SURGERY
GYNECOLOGY AND OBSTETRICS
An International Magazine, Published Monthly

VOLUME 71 AUGUST, 1940 NUMBER 2

GASTROSCOPIC OBSERVATIONS IN CASES OF GASTRIC DISTRESS FOLLOWING OPERATIONS ON THE STOMACH

HERMAN J. MOERSCH, M.D., and WALTMAN WALTERS, M.D., F.A.C.S.,
Rochester, Minnesota

GASTRIC distress which develops after an operation on the stomach often presents a difficult diagnostic problem. This is attributable to the inconsistency of symptoms and the difficulty of roentgenographic interpretation as a result of disturbance of the normal anatomy of the stomach. Any procedure, therefore, that can assist in the better evaluation of the cause of the distress deserves the most careful consideration. Gastroscopy, in our opinion, is a procedure that will be found of definite value in the study of the stomach after operation.

Schindler, in 1922, first called attention to the possible value of gastroscopy in the study of the stomach after operation. Since then, scant attention has been given to this interesting problem. It seems advisable, therefore, to present a review of the gastroscopic findings in 100 consecutive cases in which an operation had been performed on the stomach and gastric distress developed subsequently. This latter point must be especially emphasized, for this study cannot be interpreted in any way as illustrating what occurs in the average stomach following operation; rather, it is meant to demonstrate the course of events in the stomach of the patient who has subsequent gastric difficulty.

From the Divisions of Medicine and Surgery, the Mayo Clinic.

With the Wolf-Schindler flexible gastroscope it is possible to obtain a highly satisfactory view of the interior of the stomach in most cases after operation on the stomach. Many observers stress the point that orientation is much more difficult in the stomach after operation than in the intact stomach. In our experience, if the type of operation that had been performed was known before gastroscopic examination, little difficulty was encountered in this respect. In cases in which partial gastrectomy had been done, we were able to obtain a satisfactory view of the stoma in every instance. More difficulty was experienced in examining the stoma after gastroenterostomy. However, a satisfactory view could be obtained in more than 80 per cent of such cases.

Even when the entire stoma cannot be observed, a partial view, as Lintott has pointed out, can be of definite value, for "inflammatory changes present at the stoma are seldom strictly localized." Often, it is possible to observe both the gastro-enteric stoma and the antral portion of the stomach in the same gastroscopic field, and thus an opportunity is afforded to compare the peristaltic activity about the opening with that of the antrum of the stomach. Our observations are in agreement with those of Schindler (3), that the

TABLE I.—OPERATIVE PROCEDURES IN 100 CASES OF GASTRIC LESIONS

Operation and condition		Cases
Posterior gastro-enterostomy for duodenal ulcer		62
Partial gastrectomy for duodenal ulcer		19
Partial gastrectomy for gastric ulcer		3
Posterior gastro-enterostomy and knife excision for gastric ulcer		8
Resection for carcinoma		3
Miscellaneous procedures		
Knife excision for duodenal ulcer and gastro-duodenostomy	2	
Pyloroplasty for gastric ulcer	1	
Pyloroplasty for duodenal ulcer	1	
Knife excision for duodenal ulcer with reconstruction of pylorus	1	5
Total		100

Gastroscopy was performed in each of these 100 cases because of postoperative gastric distress.

peristaltic activity of the antrum of the stomach and at the gastro-enteric opening are not synchronous. Furthermore, peristaltic activity at the stoma is often absent in the presence of gastritis. Although we strongly suspect that absence of peristaltic activity at the gastro-enteric stoma may be a factor in the development of postoperative gastritis, still this is not always true. It is conceivable that a lack of activity at the stoma may occur as a result of gastritis, rather than vice versa.

The two greatest obstacles in carrying out a satisfactory gastroscopic examination after operation on the stomach are: the presence of a bubbly, bile-stained secretion which may be regurgitated through the gastro-enteric stoma and may obscure the gastroscopic field, and the placing of the stoma in such a position, especially in obese individuals, that it defies satisfactory visualization in spite of all maneuvers.

The actual amount of jejunal mucosa that can be examined in any given case through the gastroscope is dependent on the size and position of the stoma. Often it is possible to look down a barrel of the jejunum for a distance of several inches. The jejunal mucosa is readily distinguished from the gastric mucosa by its color and the regular disposition of the valvulæ conniventes.

The 100 cases to be reported are classified in Table I according to the type of operative procedure which had been employed and the condition for which the operation had been done. Gastro-enterostomy for duodenal ulcer was the most common procedure. This was to be anticipated, as it is an operation that has been employed more extensively and for a longer period than any other. Seventy-five of the patients were men and 25, women. While a slightly higher percentage of men than of women had evidence of organic disease as seen through the gastroscope, the difference was so slight in this series that it was not deemed advisable to separate the group as to sex.

OBSERVATIONS AFTER GASTRO-ENTEROSTOMY FOR DUODENAL ULCER

The gastroscopic findings in the cases in which gastro-enterostomy had been done for duodenal ulcer are given in Table II. Probably the most striking observation was that 19, or 30.6 per cent, of the patients in this group had an apparently normal mucosa. This compares closely with what was found in the series as a whole, as the stomach in 30 of the 100 cases was classified gastroscopically as normal. It is of interest to compare our observations with those of Schindler (3), who found the stomach normal in only 22.2 per cent of 1,000 cases in which routine gastroscopic examinations were performed, and only 3 of 30 stomachs examined after operation were normal. The discrepancy is more than likely to be attributable to difference of opinion as to what constitutes the borderline between the normal gastric mucosa and the early changes of gastritis. There is also the important factor of time at which the gastroscopic examination was performed. It is well known that the gastroscopic picture does not always remain constant and can change from time to time. After an acute infectious process, indiscretion in diet or other factors, there may be definite evidence of gastritis which may be absent at a subsequent examination. It might be anticipated that the longer the period of time that is allowed to elapse between operation on the stomach and gastroscopic examination, the less the likelihood of encountering gastritis. Contrary to expectation, this was not found true in our cases.

The thought naturally presents itself, what accounted for the postoperative gastric distress in the 19 cases in which gastro-enterostomy had been performed and the gastric

TABLE II.—CONDITION OF STOMACH DISCLOSED BY GASTROSCOPY AFTER VARIOUS OPERATIONS IN 100 CASES OF POSTOPERATIVE GASTRIC DISTRESS

Condition of stomach	Operation for duodenal ulcer		Miscellaneous procedures	Operation for gastric ulcer		Pyloroplasty	Resection for carcinoma
	Gastro-enterostomy	Partial gastrectomy		Gastro-enterostomy and knife excision	Partial gastrectomy		
Apparently normal mucosa	19	6	1	1	1	1	1
Gastritis	28	3	1	5	1		1
Erosive gastritis	6	9	2				
Carcinoma	2			1	1		1
Benign tumor	1						
Gastric ulcer	1			1			
Gastrojejunal ulcer	5	1					
Total	62	19	4	8	3	1	3

mucosa was normal on gastroscopic examination? In each case, the clinical history was that of an indefinite type of gastric distress, except for one case in which gastric bleeding had occurred. All patients except the one with hemorrhage were placed under medical management and their symptoms were relieved. In this group, the functional element appeared predominant. The patient with a history of gastric bleeding was subjected to partial gastrectomy. Although the patient has had no further bleeding since operation, the surgeon was unable to discern any abnormality of the gastric mucosa.

Thirty-four, or 54.8 per cent of the patients who had undergone gastro-enterostomy for duodenal ulcer, had gastroscopic evidence of gastritis. It is probably not advisable to attempt to subdivide the cases of postoperative gastritis into the various classes used for cases of gastritis of the pre-operative stomach, for practically every variety of gastritis may be seen in the same stomach (Fig. 1). There is, however, one variety which is characterized by multiple small erosions or areas of ulceration scattered throughout the gastric mucosa (Fig. 2) which, because it gives rise to more distinct symptoms and responds satisfactorily to therapeutic management, will be placed in a separate group and classified as erosive gastritis.

There were 6 cases of erosive gastritis and 28 cases of gastritis of other types in the group in which gastro-enterostomy had been performed for duodenal ulcer. The clinical course in the 28 cases of gastritis was distinctly different from that in which the gastric mucosa was normal on gastroscopic examination. In the latter group, the response to medical management was highly satisfactory. In the former the response to treatment was far from satisfactory and 7 of the 28 patients who had gastritis were subjected to subsequent gastric operation, and even then the results were not always satisfactory. In every case which came to operation, there was gross and microscopic evidence of gastritis.

Although the gastroscopist is prone to claim the domain of gastritis as his own, it is interesting to note that the roentgenologist ventured a diagnosis of gastritis in 8 of the 28 cases of gastritis after gastro-enterostomy for duodenal ulcer before gastroscopy had established that diagnosis.

In all 6 cases in this group in which a diagnosis of erosive gastritis was made, gastric bleeding had occurred at some time following gastro-enterostomy. The clinical history slightly simulated that of gastrojejunal ulcer. Because of this fact, surgical exploration for gastrojejunal ulcer was performed in 3 cases, although gastroscopic and roentgenoscopic examinations failed to reveal gastrojejunal ulcer. In all 3 cases, no gastrojejunal ulcer could be found but in each case, evidence of gastrojejunitis with multiple erosions of the gastric mucosa was found at operation.

A diagnosis of gastrojejunal ulcer was made from the gastroscopic findings in 5 of the cases in which gastro-enterostomy had been

performed for duodenal ulcer (Fig. 3). In 3 of the 5 cases surgical exploration was performed. In each case the diagnosis of gastrojejunal ulcer was confirmed both surgically and on pathological examination. In the 2 other cases medical treatment was used, so that pathological confirmation of the gastroscopic findings could not be made.

A gastric ulcer was found on gastroscopy in one of the cases in which gastro-enterostomy had been carried out for duodenal ulcer. This apparently developed 8 years after the gastro-enterostomy. The patient was placed on an ulcer diet with relief of symptoms and disappearance of the ulcer.

Two of the patients who had had gastro-enterostomy for duodenal ulcer were found to have carcinoma of the stomach on gastroscopic examination (Fig. 4). In one instance, the carcinoma involved the site of the anastomosis, and in the other the antral portion of the stomach. In both cases the gastroscopic diagnosis of carcinoma was confirmed by exploratory operation.

The final case in the group of gastro-enterostomy for duodenal ulcer was that of a tumor of the body of the stomach which gastroscopically appeared benign. This was discovered 27 years following gastro-enterostomy. Operation was advised and the tumor was removed successfully. On microscopic examination the tumor was found to be a neurofibroma.

OBSERVATIONS AFTER PARTIAL GASTRECTOMY FOR DUODENAL ULCER

The subsequent gastroscopic findings in all of the cases in which partial gastrectomy had been performed for duodenal ulcer are grouped in Table II also. In 6 of the 19 cases in this group gastroscopic examination did not reveal any abnormality of the gastric or jejunal mucosa. In this group, not so much time had elapsed between the operation and the gastroscopic examination as in the cases in which gastro-enterostomy had been performed for duodenal ulcer. The longest period of time to elapse in this group was 5 years. In the 6 cases in which gastroscopy revealed nothing abnormal, we again found that the clinical history of gastric distress was extremely indefinite, but the functional element was predominant. Again, satisfactory results were obtained through medical measures.

The most striking feature in the cases of partial gastrectomy for duodenal ulcer was the high incidence of erosive gastritis. This condition occurred in 9 of the 19 cases. At first glance, this high incidence of erosive gastritis might appear to constitute a contraindication to partial gastrectomy. Such, however, is not the case, for, as mentioned previously, this form of gastritis in our hands has responded in a most satisfactory manner to adequate medical management. In 1 of the cases of erosive gastritis, roentgenographic diagnosis of carcinoma had been made previously. Because of this, operation was performed and at operation no evidence of carcinoma was discernible but extensive erosive gastritis was noted.

In one case in this group, a gastrojejunal ulcer was suspected, but this could not be identified positively on gastroscopic examination. Roentgenographic examination of the stomach likewise failed to visualize the ulcer. The patient was operated on at home, and we were informed by the surgeon that a gastrojejunal ulcer was present.

There were three cases of gastritis following partial gastrectomy for duodenal ulcer. As in cases of gastritis following gastro-enterostomy, the response to medical management was not striking. Two of the 19 patients in this group had undergone gastric surgery before partial gastrectomy had been performed. Both had definite gastritis.

OBSERVATIONS AFTER OPERATIONS FOR GASTRIC ULCER AND CARCINOMA

There were 11 cases in which operation had been performed for gastric ulcer (Table II). In this group were 8 patients who had undergone excision of the gastric ulcer and gastro-enterostomy, and 3 who had undergone partial gastrectomy. In 2 of the cases gastroscopy failed to reveal anything abnormal. Similarly, in 2 other cases, a gastroscopic diagnosis of carcinoma was made, in 1 case 15 years after knife excision of the ulcer and gastro-enterostomy, and in the other 17 years after partial gastrectomy. Exploration was

not performed in either case after gastroscopy, so that there may be some question as to the accuracy of the diagnosis. We have been informed by the attending physician in the home locality, however, that the first patient has since died and that all the evidence pointed to carcinoma of the stomach as the cause of death. The other patient's attending physician has informed us that metastasis to the spine has developed. A diagnosis of gastric ulcer in addition to gastritis was made in 1 case. The patient was operated on and the ulcer demonstrated at operation. In the 6 remaining cases there was definite gastroscopic evidence of gastritis. In one of the 6 cases, roentgenoscopic diagnosis of gastric ulcer was made but could not be confirmed gastroscopically. The patient's symptoms were of such a nature that operation was not deemed advisable, so that the accuracy of the diagnosis was not established. In 2 of the 6 cases operations were carried out because of a history of bleeding, but nothing other than gastritis was noted in either case. In the 3 remaining cases, rather satisfactory immediate results were obtained from hospitalization and medical management.

From our limited experience, it is our impression that atrophic changes in the mucosa of the stomach are more likely to occur after partial gastrectomy than after gastro-enterostomy. Further study will be necessary, however, definitely to establish this point.

There were only 3 patients in the entire group of 100 who originally had been operated on for carcinoma of the stomach. Of these 3 (Table II) one was examined 3 months after operation and marked evidence of gastritis was found. This patient died some time later at home from what was thought to be recurrent carcinoma of the stomach. The second patient was examined 4 years after operation and found to have carcinoma involving the stoma. On exploration the lesion was found inoperable. The third patient was examined 10 years after operation and was gastroscopically normal. The patient has remained well.

MISCELLANEOUS OBSERVATIONS

Five cases which do not belong to any of the groups mentioned have been listed in Table I under miscellaneous procedures and in Table II under miscellaneous procedures for duodenal ulcer and pyloroplasty for gastric ulcer. In this group are 2 cases in which knife excision of a duodenal ulcer and gastroduodenostomy were performed. In one of these cases gastric hemorrhages developed after operation. In spite of this, gastroscopy failed to reveal anything abnormal. Because of the bleeding, partial gastrectomy was performed, and at operation nothing was found on gross examination although microscopic examination of the tissue removed revealed gastritis and duodenitis. In spite of this operation, the patient continued to have gastric difficulty. The second patient was found to have erosive gastritis on both gastroscopic and roentgenoscopic examinations. This cleared up nicely after the patient had been hospitalized and placed on adequate medical management.

The 1 patient who had undergone pyloroplasty for gastric ulcer (Table I) had never secured satisfactory relief. Gastroscopy failed to reveal any adequate explanation for the continued gastric difficulty. In spite of extensive medical management, the patient continued to have trouble. The patient who had been subjected to pyloroplasty for duodenal ulcer continued to have gastric distress with additional gastric bleeding. On gastroscopic examination, extensive erosive gastritis was discovered. Partial gastrectomy was performed and the diagnosis of erosive gastritis was confirmed.

In the final case in Table I, the patient continued with gastric distress and bleeding after knife excision of the duodenal ulcer with reconstruction of the pylorus. On gastroscopic examination extensive gastritis was noted.

SUMMARY AND CONCLUSIONS

The gastroscopic findings in 100 cases in which previous operations had been performed on the stomach and in which gastric distress developed subsequently have been reviewed. From this review, we are of the opinion that gastroscopy can be of definite assistance in reaching a better understanding of the factors that may lead to gastric distress

after operations on the stomach. Contrary to the commonly accepted teaching that gastritis is found in all stomachs after operation, in 30 per cent of this series of cases of persistent dyspepsia gastroscopic evidence of disease was not present. As a rule, in the cases in which abnormality of the gastric mucosa was not demonstrated by gastroscopy, the functional factor was found to be rather pronounced, and in most instances the patients responded symptomatically to therapeutic measures directed to this end.

In 56 cases, a diagnosis of gastritis of one type or another was made from the gastroscopic findings. In contrast to the cases in which gastroscopy revealed normal gastric mucosa, the response to medical management was not as satisfactory and many of the patients required further operation. Postoperative gastritis may be thought to be simply a manifestation of gastritis that existed before operation. No doubt this is often true, and many postoperative complications might be avoided if this possibility were always recognized before operation. On the other hand, it is known that gastritis does develop after operation, and also that gastritis which is present before operation may disappear after operation. That gastritis undoubtedly does develop after operation is seen from the fact that evidence of gastritis was present in 56 per cent of the cases in our study. In comparison, Swalm, Jackson, and Morrison found gastritis in only 35 per cent of their routine gastroscopic examinations, and Schindler (3) reported an incidence of 41.8 per cent.

It is interesting to speculate as to the possible factors responsible for postoperative gastritis. No doubt in many cases a preexisting gastritis is the responsible factor. In our opinion, a poorly placed stoma with inadequate drainage of the stomach is a very important factor and in addition, if the stoma retains an activity resembling that of a sphincter, gastritis is not as likely to develop. Infection undoubtedly constitutes an important exciting factor.

Other lesions, such as gastrojejunal ulcer, carcinoma, gastric ulcer, and benign tumor, can and do develop in the stomach after operation, and gastroscopy may be of assistance in their proper recognition. In 5 cases in our series carcinoma of the stomach was found on gastroscopic examination and in 6 cases gastrojejunal ulcer was visualized.

REFERENCES

1. Lintott, G. A. M. The practical application of gastroscopy. Proc. Roy. Soc. Med., 1939, 32: 533–542.
2. Schindler, Rudolf. Die diagnostische Bedeutung der Gastroskopie. Muenchen. med. Wchnschr., 1922, 69: 535–537.
3. Idem. The incidence of the various types of gastric disease as revealed by gastroscopic study. Am. J. M. Sc., 1939, 197: 509–516.
4. Swalm, W. A., Jackson, C. L., and Morrison, Lester. Correlation of clinical and gastroscopic findings in chronic gastritis with report of cases. Rev. Gastroenterol., 1936, 3: 219–226.

CARCINOMA OF THE STOMACH

Review of 444 Cases to Emphasize the Inadequacy of Present Methods for an Early Diagnosis

ROBERT H. ABRAHAMSON, M.D., and J. WILLIAM HINTON, M.D., F.A.C.S.,
New York, New York

INVESTIGATION of cases of gastric carcinoma in which patients were admitted to a hospital in a large urban center reveals many interesting, if disturbing, facts. During the past two decades—1919 to 1938 inclusive—the medical and surgical wards of the Fourth Division of Bellevue Hospital admitted 444 patients with cancer of the stomach, of whom 31 were readmissions. Total admissions to Bellevue Hospital during this 20 year period were 1,040,784, indicating that about 0.17 per cent of the patients admitted suffered from cancer of the stomach.

During these two decades, a great many more gastric carcinoma cases were discharged than have been reported. It is certain that both by clinical and clerical errors, many discharges have been listed and filed under other diseases, i.e., bronchopneumonia, unknown disease, metastatic carcinoma primary unknown, etc. Insufficient clinical data and no pathological, roentgenological or surgical proofs were found in the records of 40 patients discharged as gastric carcinoma, for which reason such data were omitted.

Since cancer of the stomach accounts for approximately one-third of the total deaths due to cancer in the United States, the problem of the end-results in these cases is extremely important. The dismal picture shown in our statistics illustrates the necessity of a more general approach to the problem. We feel that a statistical study of this group will give a more correct evaluation of the end-results in this type of carcinoma than the usually more optimistic surveys from clinics which tend to see selected cases from the country at large.

OPERABILITY AND MORTALITY

Of the 444 cases of gastric carcinoma, 296, or two-thirds, were inoperable on admission, and of these 36 patients were moribund, succumbing within 48 hours despite every effort to prolong their lives (Chart 1). Age, extreme cachexia, or a lesion deemed too extensive by clinical examination for removal caused 80 patients to be classified as "unjustifiable risks." Of these, 44, or 55 per cent, died while on the wards. In 105 cases there were evident metastases—by clinical examination—i.e., jaundice, enlarge cervical nodes, etc. Despite favorable clinical opinion, in 40 cases x-ray examination showed a lesion inoperable because of extent or location, and in 19 additional instances the x-ray showed metastases rendering operative cure impossible. In 52 cases operation was refused. In a number of cases the carcinoma was inoperable for more than one of the reasons mentioned.

After clinical and x-ray examination, 148, or 33⅓ per cent, of the patients were considered operable. Apparently some improvement in their condition could be hoped for after surgical intervention. However, even in this group, exploratory laparotomy in 69 cases proved that no further operative measure could be undertaken. Of these, 34, or 46.6 per cent, succumbed following operation.

In 55 cases palliative operations were performed: gastrostomy in 5, jejunostomy in 9, closure of perforation in 3, 1 secondary operation for recurrent carcinoma of the stomach following gastrectomy was attempted, but death resulted, gastro-enterostomy was performed in 37 cases. The particular palliative procedure selected made little difference in the fate of the patients, since we know that practically all of them died within a year. The only purpose of the operation was temporary relief of an obstructive lesion. Fourteen patients were reported as improved after gastro-enterostomy and discharged from the hos-

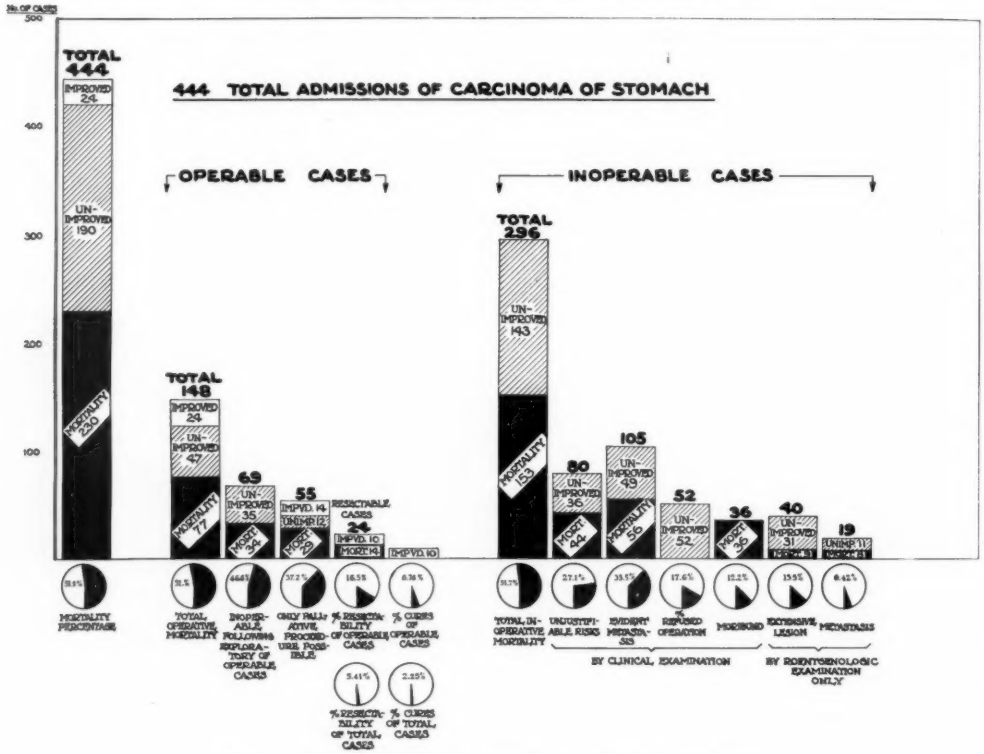


Chart 1. Comparative results of operable and inoperable carcinoma.

pital as such, but this improvement we know was a very temporary one.

In only 24 cases of the total of 444 was it possible to resect the carcinoma. In this group, there were 14 deaths following the operation.

Our statistics show that only 24 cases of the total of 444, or 5.4 per cent of the total and 16.2 per cent of the 148 operable cases, could be subjected to gastric resection, the only hope for effecting a permanent cure in gastric carcinoma.

The mortality statistics indicate that deaths accounted for over half the cases in both the inoperable and the operable groups. Of the inoperable cases, 153 died without benefit of surgical intervention; of the operable cases, 77 were operative mortalities. These statistics reveal the low possibility of cure for the patient who enters a general hospital with carcinoma of the stomach, and are probably a fair index of conditions in similar hospitals throughout the world. We realize that our percentage of resectability (5.4 per cent) is in no way comparable to figures reported by certain of our large clinics where cures of as many as 20 per cent of cases have been shown. These favorable reports from large and well known surgical centers are apparently the results of gastric resections in a carefully selected group of cases. The majority of such patients are referred to these centers by private physicians who have already chosen them as particularly favorable prospects for operation. The obviously inoperable cases never reach the large clinics. This factor of selection, we feel, accounts for the wide divergence in the statistical results which have been arrived at by these clinics and the general hospitals.

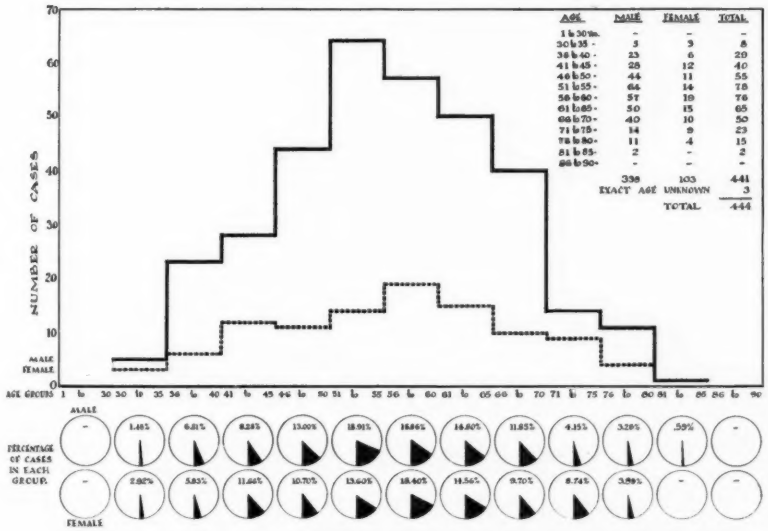

NUMBER OF CASES
AGE GROUPS
MALE
FEMALE
PERCENTAGE OF CASES IN EACH GROUP.
AGE | MALE | FEMALE | TOTAL
1 to 30 yrs. - - -
30 to 35 - 3 3 6
36 to 40 - 23 6 29
41 to 45 - 28 12 40
46 to 50 - 44 11 55
51 to 55 - 64 14 78
56 to 60 - 57 18 76
61 to 65 - 50 15 65
66 to 70 - 40 10 50
71 to 75 - 14 9 23
76 to 80 - 11 4 15
81 to 85 - 2 - 2
86 to 90 - - - -
EXACT AGE 338 103 441
UNKNOWN 3
TOTAL 444

Chart 2. The incidence of male and female admissions, divided into age groups.

DIAGNOSIS

Age and sex factors. In our series there were 341 cases in males and 103 in females, a ratio of approximately 3 to 1 (Chart 2). This great preponderance of males has been corroborated in many other reports. It is a well known fact (as seen from Chart 2) that the great majority of gastric carcinomas occur between the forty-fifth and sixty-fifth years. In our series the peak of incidence in males occurs between 51 and 55 years of age and that in females between 56 and 60 years of age. These findings concerning the preponderance in males and the incidence in later life are the two outstanding, unexplained factors in this condition. During that period of life when carcinoma most often occurs, there are marked changes in the content and nature of the sex hormones. This is evidenced by their chemical recovery from the blood and urine and by the involutionary changes which take place during this period. An effort to correlate these facts is being attempted in a further publication.

Symptomatology. The presenting symptoms in those patients admitted to our wards with gastric carcinoma are: pain, 92.8 per cent; loss of weight, 89.6 per cent; weakness, 60.5 per cent, and cachexia, 43.7 per cent; jaundice, 23.2 per cent; nausea and vomiting, 16.3 per cent; and hematemesis, 9.2 per cent. It is evident that jaundice is a late and unfavorable symptom. However, the great majority of cases in which jaundice had not occurred, could not be considered as favorable, since even though they received prompt attention (clinical, diagnostic, and surgical) they often proved inoperable (Chart 3): 66⅔ per cent, 296 cases presenting these symptoms, proved inoperable; 83.5 per cent, or 124 of those considered favorable prior to operation, were found by exploration to be inoperable or subject only to palliative operation.

Perhaps even more significant is our finding that the duration of symptoms had practically no relationship to the resectability or operability of the lesion. From Chart 3, it is clear that approximately the same percentage of inoperable cases were discovered in the group in which symptoms had been present for 1 month or less, as in groups in which symptoms had been present for a year or more. Apparently, our closely held belief, that cases in which the symptomatology is recent in development hold a better prognosis, is in gastric carcinoma, at least, nothing more than a

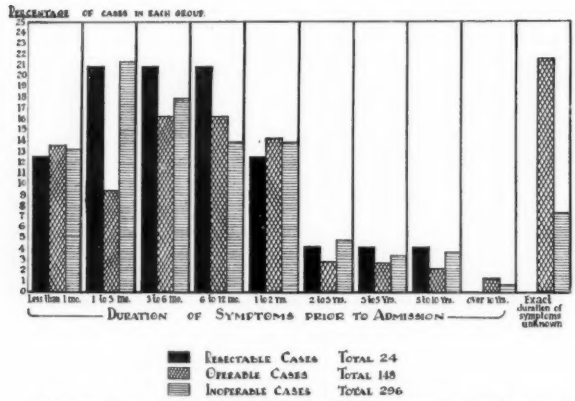

Percentage of cases in each group
Less than 1 mo.
1 to 3 mo.
3 to 6 mo.
6 to 12 mo.
1 to 2 yrs.
2 to 5 yrs.
5 to 5 yrs.
5 to 10 yrs.
over 10 yrs.
Exact duration of symptoms unknown
Duration of Symptoms prior to Admission
Resectable Cases Total 24
Operable Cases Total 148
Inoperable Cases Total 296

Chart 3. The relationship of the duration of symptoms in the resectable, operable and inoperable groups . . . as indicated by percentages.

shibboleth. No matter how long symptoms have been present, our statistics show a startling similarity of the percentage possibility of improvement by operation (Chart 3).

It is enlightening to note that in the groups in which the duration of symptoms was less than 3 months both the percentage of resectable and the percentage of operable cases were smaller than the percentage of inoperable cases. Presumably a cancer so malignant as to produce troublesome symptoms in so short a time progresses too rapidly to be operable. It is obvious that our criteria for diagnosis of gastric carcinoma are faulty, and that the symptomatology we depend upon is unreliable for early diagnosis. If we wait for these evidences, we are allowing the patient to pass the stage at which complete surgical removal with possible cure can be offered. Our present accomplishment is that of making a determined effort to diagnose the late cases.

Peptic ulcer. In 55 of our cases, a clinical diagnosis of ulcer had been made, and in 21 additional cases it was reported after x-ray examination. In the 368 cases remaining there was no evidence in the clinical history, the report of the physician, or the x-ray examination that a diagnosis of peptic ulcer had ever been suggested.

We had only 17.1 per cent of cases in which a malignant degeneration of peptic ulcer could be considered as possible. Many authors have considered this change as likely (1, 3, 6, 11, 12, 17, 19). Smithies and Ochsner (17), in a résumé of 566 cases, reported that 239, or 41.8 per cent, fell into the "cancer following ulcer" category. Early gastric carcinomas may appear in their early stages as small ulcerative lesions on roentgenological examination. During this period, they may give every sign and symptom of gastric ulcer—they are gastric ulcers at this stage. However, there is no proof on examination either of operative or autopsy material, as shown by Ewing (5), that these malignant ulcers had their inceptions as benign ulcerative lesions. Their malignancy becomes apparent upon further involvement of the stomach and its adjacent organs or upon the appearance of distant metastases.

The more frequent use of the gastroscope has shown that gastric malignancy occurs on mucosa which is already the seat of a chronic pathological alteration (2, 4, 13, 16). However, this lesion so far as we have been able to ascertain is not a peptic ulcer.

Gastric ulcer and gastric carcinoma have entirely individual and clearly typical clinical and pathological manifestations which bear little relationship to each other. Both lesions are of fairly common occurrence, and it is therefore not surprising that in some cases they may be found concomitantly. Such coincidences are not proof that one condition has developed *as a result* of the other. "It is conceivable that these two entities may be

linked by etiological relationship." A review based on experimental work on the effects of hormones on the gastric mucosa and the pathological states which they institute will be published at a later date. As yet, there is little proof established that malignant ulceration has originally been benign. In a previous report (7) from our clinic we found on studying 104 gastric ulcers and 118 gastric carcinomas, that 9 ulcer cases were suggestive of carcinoma, and immediate operation was advised. One refused and 8 were operated upon. Six of the eight were proved histologically to be benign. In over 1,000 cases of peptic ulcer followed from 1 to 12 years, we have not observed this transformation to take place. From our clinical experience in observing gastric ulcers, we feel that the indication for immediate operation as a means of preventing malignant degeneration is seldom present.

X-ray diagnosis. A gastro-intestinal series of x-ray diagnosis was carried out in 265 of our series of 444 cases. A number of patients were unsatisfactory subjects because their moribund condition, vomiting, hematemesis, etc. made them too ill for this type of examination.

Of the 265 cases in which x-ray was done, 237 showed roentgenological evidence of carcinoma of the stomach. The 28 remaining were reported as negative for gastric carcinoma, but laparotomy proved the existence of the lesion.

By arbitrarily dividing the cases into 4 groups, according to the extent and locality of the lesion, it was found that 74, or 28 per cent, were located unfavorably for radical resection. One hundred thirty-three cases showed roentgenological evidence of carcinoma involving more than a single portion of the stomach and were unfavorable because of the extent of the lesion.

In group 1, 12 showed involvement of the esophagus by extension, 44 in the cardia, and 3 in the fundus. In group 4, the lesion was shown to be large and extensive, in each case involving more than one-half of the stomach. These (groups 1 and 4) were obviously unfavorable subjects for extirpation of the entire lesion. The 2 remaining groups—2 in which the lesser or greater curvature or media was involved and 3 in which the pylorus was the seat of the lesion—were considered more hopeful. Another complicating factor was that the lesion had not remained localized in the affected site but had advanced beyond it. In 56 cases, 22.2 per cent, the carcinoma involved both sites mentioned in groups 1 and 2. Thus the favorable outlook was considerably lessened.

Gastric analysis. Gastric analysis was performed in 70 of our cases, of whom 60 showed absence or diminution of free hydrochloric acid. In 46 cases blood was present.

Because of its simplicity, the gastric test meal should be carried out as a routine procedure among patients in the so called cancer period. In patients with achlorhydria, x-ray examinations should be repeated often to enable recognition of the earliest possible sign of change.

Certainly one cannot generalize that all patients with achlorhydria and achylia fall into the classification of gastric carcinoma, but such findings ought to stimulate a suspicious attitude. The strong possibility of cancer is to be kept in mind until roentgenological or gastroscopic examination definitely excludes it.

In every patient with vague abdominal complaints who has passed his thirty-fifth year, and in whom a diagnosis is not obvious, gastric malignancy must be ruled out. The most dependable means at our disposal for this purpose are the gastric test meal, the fluoroscopic and x-ray examination, and gastroscopy. The x-ray evidence has already been indicated for this series. However, it is noted that x-ray films are taken too infrequently and are not repeated. The physician has often been limited in his examination of the patient because of the expense of the procedure (although this expense could and should be materially reduced).

Gastroscopy. The advent of the flexible gastroscope has widened the diagnostic possibilities in gastric carcinoma. At present many well trained men are perfecting this technique so that it may become available as a deciding factor in disputed and undiagnosed cases. When a decision is obscure following clinical, roentgenological and laboratory studies, the

patient should have the benefit of a gastroscopic examination.

SUMMARY AND CONCLUSIONS

1. The outlook in gastric carcinoma is at the present time a very dismal one, since the largest number of patients in whom the diagnosis is made are already in an inoperable stage. Often when operability still exists, resectability is impossible. The percentage of successful cures in a general hospital remains very small.

2. Large surgical centers are enabled to show a better result because of preliminary selection of cases by the referring physician.

3. The most dependable confirmations of diagnosis are the x-ray, the gastroscope, and the gastric test meal. The latter is the simplest and may be repeated at frequent intervals at relatively little expense. When examination shows a declining gastric acidity, the suspicion of carcinoma must be entertained and disproved.

4. Roentgenological studies of the stomach should be made with greater frequency. The physician must arrange with roentgenologists for lowered cost of this procedure so that such examination may be done repeatedly in suspicious cases and in those comprising the large group with undiagnosed and vague manifestations. X-ray of these patients is necessary, not to verify an already made clinical diagnosis, but for careful search where there is no evidence or only minimal evidence of gastric pathology.

5. The technique of gastric resection has been perfected in the hands of those who have the opportunity of performing this operation frequently. Further operative refinements cannot offer hope for lengthening the life span of gastric carcinoma patients. Their hope resides in the development of a means of diagnosis which will permit surgical intervention when the lesion is pathologically young rather than early in the clinical course.

6. Several authors (7, 10, 14, 15, 18) have pointed out that certain gastric malignancies are radiosensitive and have suggested combined forms of therapy. However, this is admittedly merely palliative. Levin has tried roentgen therapy in a number of cases and discarded the method completely, although he still believes in the insertion of radon into inoperable growths at operation. Radiotherapeutic methods in the treatment of gastric carcinoma may be envisioned, but this possibility offers little immediate hope.

7. The knowledge of the present dark outlook of the patient with carcinoma of the stomach should be disseminated among all practitioners and students of medicine. Until more specific tests are developed, each patient should have the benefit of such methods as are at our disposal. Faithful use of the test meal, the x-ray, and the gastroscope may help us to disclose early carcinomatous lesions.

8. Experimental and investigative endeavors to explain the sex linkage and age incidence in gastric carcinoma should be attempted. In view of recent biochemical and physiological discoveries, a new field is opened to those who are studying the etiology of carcinoma.

REFERENCES

1. Adami, J. G. The Principles of Pathology. Chapter on Malignancy, Vol. 1, p. 616. Philadelphia: Lea & Febiger, 1908.
2. Blackford, J. M. Gastric symptoms; an analysis of one thousand cases. J. Am. M. Ass., 1921, 77: 1410–1412.
3. Chang, H. C. Incidence of malignancy in gastric ulcer. Am. J. Digest. Dis., 1936, 3: 10–12.
4. Davis, T. D., and Vanderhoof, D. A study of the causes of indigestion based on our analysis of 4,000 consecutive cases. Virginia M. Month., 1926–1927, 53: 446–448.
5. Ewing, J. The beginning of gastric cancer. Am. J. Surg., 1936, 31: Feb.
6. Graham, C. Prominent symptoms in the diagnosis of gastric and duodenal ulcers. J. Am. M. Ass., 1908, 51: 651–653.
7. Hinton, J. W., and Trubek, M. The transformation of gastric ulcer into gastric carcinoma. Surg., Gynec. & Obst., 1937, 64: 16–21.
8. Holmes, G. W., and Hampton, A. O. Incidence of carcinoma in certain ulcerating lesions of the stomach. J. Am. M. Ass., 1932, 99: 905–907.
9. Judd, E. S. Jr. Quoted by Alvarez, W. C. Gastritis. Am. J. Digest. Dis., 1939, 6: 209–210.
10. Levin, I. Intraperitoneal insertion of radon and gastroenterostomy in carcinoma of the pyloric end of the stomach. Am. J. Roentgenol., 1935, 34: 69–76.
11. Levine, I. Changes in the tissue surrounding a growing tumor and the significance of the precancerous state. J. Exper. Med., 1912, 16: 149–164.
12. MacCarty, W. C. Pathology and clinical significance of stomach ulcer. From a study of the material from 216 partial gastrectomies for ulcer, ulcer and carcinoma, and carcinoma. Surg., Gynec. & Obst., 1910, 10: 449–462.

13. McNeer, G., and Barowsky, H. A gastroscopic study of the incidence of chronic gastritis in common gastric afflictions. Am. J. Digest. Dis., 1939, 6: 180–182.
14. Pettit, R. T. Carcinoma of the stomach. Diagnosis and a suggested plan of treatment. Am. J. Digest. Dis., 1939, 6: 176–179.
15. Pohle, E. A. Clinical Roentgen Therapy. P. 226. Philadelphia: Lea & Febiger, 1938.
16. Schindler, R., Ortmayer, M., and Renshaw, J. F. Chronic gastritis. J. Am. M. Ass., 1937, 108: 465–467.
17. Smithies, F. Cancer of the Stomach. Philadelphia and London: W. B. Saunders Co., 1916.
18. Waters, C. A., in discussion on Merritt, E. A. Radiation therapy of inoperable intra-abdominal malignancy. Am. J. Roentgenol., 1936, 36: 330–331.
19. Wilson, L. B., and MacCarty, W. C. The pathology relationships of gastric ulcer and gastric carcinoma. Am. J. M. Sc., 1909, 138: 846–852.

DANGERS OF THE INDISCRIMINATE COVERANCE OF PARENTERALLY ADMINISTERED GLUCOSE WITH INSULIN

PAUL CHADBOURNE ESCHWEILER, M.D., Brooklyn, New York

THE "routine" administration of insulin during intravenous infusion of solutions of glucose is often fraught with danger. Too often there is complete disregard of the patient's intrinsic mechanism of carbohydrate utilization and of the potential stimulating effect of the glucose alone on this mechanism. Most physicians advocate that whenever a patient with diabetes mellitus complicated by a surgical or obstetrical condition is given an infusion of 500 cubic centimeters of 10 per cent glucose, 25 units of regular insulin should be administered to "cover" the glucose as a routine measure. This teaching has led to the impression that the status of the diabetes can be disregarded because the action of the insulin is nullified by the parenterally administered glucose.

The fact that all patients with diabetes mellitus cannot tolerate the same amount of insulin with an infusion of glucose without suffering hypoglycemic reactions was made evident by 2 cases which were presented at medical conferences during the past year. Two patients with moderate diabetes mellitus had severe hypoglycemic reactions following glucose infusions "covered" by insulin administered subcutaneously. One, a female aged 48 years who was known to have had diabetes for 8 years, had not strictly adhered to the prescribed diet and had been given insulin at various periods. The patient was admitted to the hospital with a history indicative of cholecystic disease, which was later confirmed by roentgenogram and laparotomy. Before operation was performed good control of carbohydrate metabolism was obtained by a prescribed diet of 170 grams of carbohydrate, 75 grams of protein and 50 grams of fat without insulin. The operation was done under gas-oxygen-ether anesthesia. Following operation 700 cubic centimeters of 10 per cent glucose was administered intravenously accompanied by 35 units of regular insulin which was injected subcutaneously. Within 2 hours marked manifestations of hypoglycemia occurred. The condition resembled postoperative or anesthesia collapse with respiratory center depression.

The second patient was a gravid female, aged 30 years, who was known to have had diabetes for 6 months. The condition had been well controlled by means of a diet of 190 grams of carbohydrate, 79 grams of protein, and 45 grams of fat with 15 units of regular insulin a day. She was admitted to the hospital near term for an elective cesarean section. As a pre-operative "routine" procedure 1000 cubic centimeters of 10 per cent glucose was given intravenously and 50 units of regular insulin subcutaneously. After operation hypoglycemia was evidenced by convulsions, characterized by a decerebrate attitude. The

From the Brooklyn Hospital and Diabetic Clinic, Methodist Hospital.

blood sugar taken at this time was below 10 milligrams per 100 cubic centimeters of blood.

The untoward responses in both cases indicate that there is a real danger of a severe insulin reaction in patients with mild or moderate diabetes mellitus who receive infusions of glucose "covered" by regular insulin. Prompted by these observations 5 patients with diabetes mellitus in various degrees of severity were given infusions of 500 cubic centimeters of 10 per cent glucose in saline solution *without insulin*. One additional patient, a non-diabetic, served as a control. The blood sugar curves of each were plotted. Four of the patients had been admitted to the hospital for infections of the feet which healed under conservative treatment; 1 had been admitted for dietary and insulin adjustment. The diet for all 5 patients had been moderately high in carbohydrates (160 to 220 grams) and low in fats (45 to 57 grams) and proteins (76 to 82 grams) for at least 2 weeks before the glucose infusion was administered. The patients were not allowed to eat breakfast before the intravenous glucose tolerance test was made and in each case any prescribed insulin was omitted. (No member of the group was receiving protamine insulin.) An infusion of 10 per cent glucose in saline solution was given to each patient at a constant rate of flow so that 500 cubic centimeters was administered in 30 minutes. Determinations were made before and during the administration of the glucose and samples were taken for each patient at the close of the 30 minute period and every 30 minutes thereafter. All of the determinations of blood sugar were made by the same technician, who employed the modified Benedict's micro-chemical method (9). The results of the determinations are charted in Figure 1.

It will be observed that the most severe case of diabetes mellitus, represented by curve I, had a fasting blood sugar of 425 milligrams per 100 cubic centimeters of blood. At the close of the 30 minute period of infusion it rose to 800 milligrams. Within 1½ hours after completion of the infusion, the blood sugar dropped to within 100 milligrams of the fasting level. The mildest case (curve V) had a fasting blood sugar of 140 milligrams. The blood sugar rose to 425 and returned to within 10 milligrams of the fasting level in 1½ hours and dropped to 100 milligrams or 40 below the fasting level in 3½ hours. At the completion of the infusion all the curves show a sharp break and then, with the exception of curve VI, have a similar downward trend, the values depending on the height of the fasting level. Characteristically, curves I, II, III, and IV, which represent the more severe cases of diabetes, do not descend as abruptly as curve VI which represents the case without diabetes. As expected, the patient with mild diabetes (curve V) tends to approach the levels of the non-diabetic. This analysis, therefore, would indicate that following an infusion of 500 cubic centimeters of 10 per cent glucose even a patient with severe diabetes mellitus does not require regular insulin to return the blood sugar values near to the fasting level.

REVIEW OF THE LITERATURE

McKittrick and Root and many other writers have studied the management of patients with diabetes mellitus complicated by surgical or obstetrical conditions, the diet prescription, and use of insulin, glucose infusions, physiological saline or Ringer's solution for dehydration, or R-lactate for acidosis. However, I have been unable to find in the literature any previous report of blood sugar response following glucose infusions or the danger of routine use of insulin to "cover" glucose administered parenterally.

The danger of hypoglycemia, especially in individuals with arteriosclerosis, has been excellently studied by Middleton and Oatway and by many other writers.[1] Deaths due directly to insulin reactions have been reported (3).

The intravenous injection of glucose increases carbohydrate utilization. The increase is probably due to stimulation of endogenous insulin production or depression of the anti-insulin factor of the pituitary gland. Depisch and Hasenoehrl have shown that intravenous injection of glucose in non-diabetic subjects produces a hyperglycemia followed by hypoglycemia. It is also demonstrated in this study by the drop in blood

[1](2, 4, 5, 7, 8, 12, 14, 18-21, 23, 26)

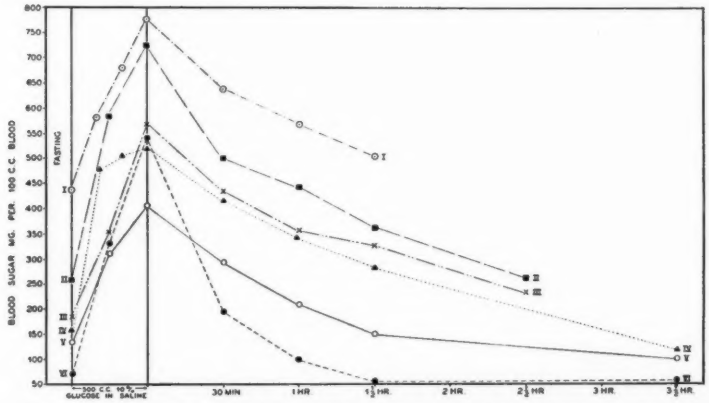


Fig. 1. Blood sugar curves following glucose infusion without insulin. Curves I, II, III, IV, and V represent patients known to have diabetes mellitus. Curve VI represents a patient without diabetes mellitus. Blood sugar levels approximate their usual fasting levels in 1¼ to 2 hours after infusion and sink to the fasting levels or lower within 3½ hours.

sugar below the fasting level in curves V and VI. Weber and Hausler believe that the drop to a value below the fasting level is due to an increased secretion of insulin. In their experiments they found that the blood sugar level ultimately sinks lower in normal subjects injected with regular insulin administered subcutaneously with an intravenous injection of glucose than in the same subjects given an equal amount of insulin and *no glucose*. These findings are in keeping with the work of Staub and Traugott who independently determined the effect of glucose given orally on the blood sugars of diabetics and non-diabetics. The glucose was administered in single doses and in 2 doses divided by a lapse of time. A single dose of glucose given orally to a non-diabetic at first caused an elevation of the blood sugar level. It then began to drop and within 2 hours after the administration of the glucose the blood sugar was below the fasting level. A second dose given during the descent of the curve either caused only a slight elevation of the blood sugar level or none at all in the patient without diabetes. In a patient with diabetes mellitus the second dose caused a further rise in the blood sugar. Individuals with diabetes lose in varying degree the ability to respond with insulin production to stimulation by carbohydrates. The amount of the rise in blood sugar following the second dose in the patient with diabetes mellitus varies inversely with the degree to which the individual's glucose utilization mechanism is stimulated. The milder the diabetes, the more nearly does the response approach that of the non-diabetic patient.

"Insulin-like" reactions may occur with blood sugar values over 200 milligrams per 100 cubic centimeters of blood. Reactions from regular insulin given subcutaneously in these unusual cases are evidently due to rapid drop of blood sugar; that is, a patient with a blood sugar of 350 milligrams which suddenly drops to 200 milligrams following regular insulin administration may go into shock (24).

A plea to individualize the treatment of patients with diabetes mellitus will bear reemphasis. The great variation in the diabetic status is evident when the definition of true diabetes mellitus as given by Joslin is considered: First, any patient who has glycosuria demonstrable by any of the common laboratory tests is considered to have diabetes mellitus until the contrary is proved. Second, any patient with a fasting blood sugar above 140 milligrams per 100 cubic centimeters of blood on an unrestricted diet, or 170 milligrams or more after a meal with a simultaneous glycosuria plainly related to diet, is a true diabetic. Obviously many patients with diabetes mellitus present only have mild cases and closely

approach the normal. The fasting blood sugar levels range from these lower limits to over 500 milligrams per 100 cubic centimeters of blood with or without fasting glycosuria. The range of the fasting levels of the blood sugars is demonstrated in this study (Fig. 1, curves I, II, III, IV, and V).

Not only is the severity of diabetes mellitus an important factor to be considered before the administration of glucose *with* insulin, but also the fact that the patient's ability to utilize carbohydrates varies at different times during the day. An excellent example of this is the blood sugar changes, studied by Barach, that occurred in a patient with diabetes mellitus after he had had breakfast. The patient was a 57 year old male known to have had diabetes for 1 month. He had been on a diet of 200 grams of carbohydrate, 70 grams of protein, and 85 grams of fat without insulin for the 8 days prior to the day blood sugar determinations were made at hourly intervals. Fasting blood sugar was 200 milligrams per 100 cubic centimeters of blood. This rose to 300 milligrams 2 hours after breakfast and in 1 hour dropped to 120 milligrams, a sudden drop in his blood sugar of 180 milligrams in 1 hour *without* parenterally administered insulin. Fluctuations in blood sugar levels are found particularly in the child with diabetes and also at the other end of life when arteriosclerosis is common.

It is frequently impossible to individualize the treatment of a patient with diabetes mellitus when the patient is being admitted for emergency surgery. A case of mild diabetes frequently has a pre-operative glycosuria of 2 to 3 per cent with a blood sugar level of 190 to 250 milligrams per 100 cubic centimeters of blood. Such findings would lead one to believe that the patient had severe diabetes mellitus and would therefore tolerate large doses of regular insulin. These patients of unknown status run the grave danger of insulin reactions when an infusion of glucose is arbitrarily "covered" with regular insulin.

To make the statement that 1 unit of regular insulin will metabolize 2 grams of glucose is to invite trouble. Joslin says, "It is dangerous to prescribe insulin in arbitrary or schematic fashion. In general the method of trial and error should be adapted, always erring on the side of low and frequent rather than high and single dosage. In general 1 unit of insulin will metabolize 1 to 2 grams of carbohydrate and perhaps even 3 to 6 grams." Newburgh says that 1 unit of regular insulin will metabolize 7 grams of carbohydrate and Holm makes the statement that 8.75 grams of carbohydrate are metabolized by each unit of regular insulin.

A factor of extreme importance is the degree of sensitivity to insulin, and this must ever remain an unknown variable. Himsworth has demonstrated that different cases of diabetes mellitus given equivalent amounts of regular insulin intravenously and glucose orally register marked differences in blood sugar responses.

SUMMARY

A usual pre-operative or postoperative procedure is to give an infusion of 500 cubic centimeters of 10 per cent glucose "covered" by 25 units of insulin in cases of diabetes mellitus complicated by obstetrical or surgical conditions. Too frequently a hypoglycemic reaction results. Therefore, a study has been made to determine whether all patients with diabetes mellitus can be expected to tolerate the same amount of insulin with an infusion of glucose. Intravenous glucose tolerance tests were given to 5 patients with diabetes mellitus of various stages of severity and to 1 normal patient. It was determined that insulin is not required to reduce the blood sugar values near to the fasting level after the intravenous administration of 500 cubic centimeters of 10 per cent glucose, as the blood sugars of the patients with diabetes mellitus reached blood sugar levels approximating their usual fasting levels within 1½ to 2 hours. It was demonstrated that the milder the case of diabetes the more nearly was approached the curve representing the non-diabetic patient. It may be concluded, therefore, that insulin should never be *routinely* administered to "cover" parenterally administered glucose in patients with diabetes mellitus. The diabetic status of the patients must be taken into consideration and thus dangerous hypoglycemic reactions may be avoided.

BIBLIOGRAPHY

1. Barach, J. H. Ann. Int. Med., 1937, 10: 1335.
2. Blake, K. W. J. Am. M. Ass., 1937, 108: 443.
3. Bowen, B. D., and Beck, G. M. Ann. Int. Med., 1933, 6: 1412.
4. Collens, W. S., Stoliarsky, R. G., and Nelzer, S. Am. J. M. Sc., 1936, 191: 503.
5. Cruickshank, E. W. H., and Startup, C. W. J. Physiol., 1933, 77: 365.
6. Depisch, F., and Hasenoehrl, R. Klin. Wchnschr., 1926, 5: 2011.
7. Ernstene, A. C., and Altschule, M. D. J. Clin. Invest., 1931, 10: 521.
8. Gigon, A. Schweiz. med. Wchnschr., 1923, 53: 882.
9. Hawk and Bergeim. Practical Physiological Chemistry. P. 436. Philadelphia: P. Blakiston & Son, 1937.
10. Himsworth, H. P. Lancet, 1936, 230: 127.
11. Holm, K. Arch. f. exper. Path. u. Pharmakol., 1927, 121: 386.
12. John, N. J. Ohio State M. J., 1937, 33: 741.
13. Joslin, E. P. The Treatment of Diabetes Mellitus. 5th ed., pp. 17, 285. Philadelphia: Lea & Febiger, 1935.
14. Lymburner, R. M. Proc. Staff Meet. Mayo Clin., 1933, 8: 235.
15. McKittrick and Root. Diabetic Surgery. Philadelphia: Lea & Febiger, 1928.
16. Middleton, W. S., and Oatway, W. H., Jr., Am. J. M. Sc., 1931, 181: 39.
17. Newburgh, L. H., and Waller, D. S. J. Clin. Invest., 1932, 11: 995.
18. Nicely, W. E., and Edmondson, C. C. Am. J. M. Sc., 1924, 167: 570–586.
19. Root, H. F. Ann. Int. Med., 1938, 11: 1332.
20. Sherrill, J. W. Calif. & West. Med., 1933, 38: 73.
21. Soskin, S., Katz, L. N., Strouse, S., and Rubinfeld, S. H. Arch. Int. Med., 1933, 51: 122.
22. Staub, H. Cited by Joslin, E. P. loc. cit. (13). The Treatment of Diabetes Mellitus, 5th ed., p. 100. Philadelphia: Lea and Febiger, 1935.
23. Strouse, S., Soskin, S., Katz, L. N., and Rubinfeld, S. H. J. Am. M. Ass., 1932, 98: 1703.
24. Sunderman, F. W., Austin, J. H., and Williams, P. J. Clin. Invest., 1932, 11: 1261.
25. Traugott, K. Klin. Wchnschr., 1922, 1: 892.
26. Tuttle, E. New York State J. Med., 1937, 37: 636.
27. Weber, R., and Hausler, H. Klin. Wchnschr., 1927, 6: 1521.

RENAL DISPLACEMENT

M. MUSCHAT, M.D., F.A.C.S., and L. EDEIKEN,
Philadelphia, Pennsylvania

IN this study we have attempted to correlate the various findings of renal displacement by the adjacent organs and of the reverse, namely, the displacement of the adjacent organs by the kidney in diseased states. The findings presented are based on the actual conditions found by x-ray and in most instances proved by operation or autopsy. This study was divided into two parts: (1) The displacement of the kidney by the adjacent organs, and (2) the displacement of the adjacent organs by the kidney.

While proceeding with this work every organ adjacent to the kidneys was studied, and observations were made as to its influence in displacing the kidney in varied pathological states.

RENAL DISPLACEMENT BY THE ADJACENT ORGANS

The kidney, like any other organ, may be displaced from its original bed by the encroaching massive pressure of a neighboring structure. This displacement, however, does not occur always and is apparently limited by certain anatomical factors. One mass may displace it, while another in the same position will not dislodge it from its bed.

From the Departments of Urological Surgery and Radiology, Mt. Sinai Hospital and the School of Medicine, University of Pennsylvania, Philadelphia, Pennsylvania.

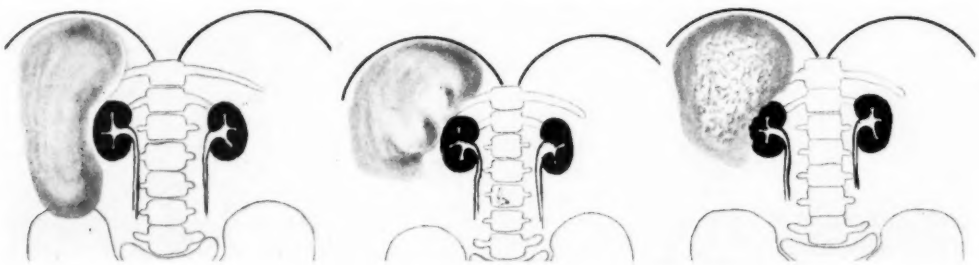
Liver. It is surprising that the liver with its bulk in massive enlargement does not displace the kidney. We observed no displacement in hepatomegaly, huge carcinomatous tumor, and large hydatid cysts (Fig. 1).

Spleen. The spleen may and may not displace the kidney. If the splenic mass becomes enlarged in all directions like in splenic infarct or lues, it will always displace the kidney downward and inward, bringing it to lie on top of the transverse processes of the vertebræ. If, however, the spleen enlarges downward only, that is, intraperitoneally, displacement is absent or may be very slight (Fig. 2).

Pancreas. Recently Kretschmer[1] reported a rare case of a large pancreatic cyst proved by operation. There was a very notable displacement of the kidney downward and outward (Fig. 2d).

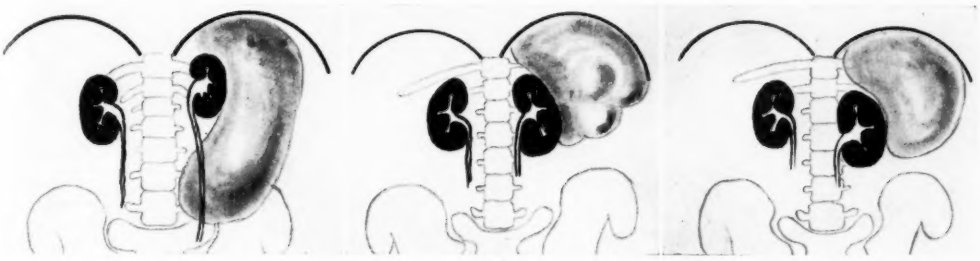
Retroperitoneal tumor. Every retroperitoneal tumor will displace the kidney, moderately at first and very markedly as the size of the tumor increases. The kidney can be displaced mesially, downward, upward, and outward, depending upon the location of the tumor either laterally, above, or below the kidney. If the tumor is a solid unattached fibrosarcoma below the kidney, it will dislodge and rotate it with the calyces pointing straight upward (Fig. 3).

[1]Surg., Gynec. & Obst., 1939, 69: 671.



a b c

Fig. 1. a, Hepatomegaly; b, carcinoma of liver; c, hydatid cyst of liver.



a b c

Fig. 2. a, Splenomegaly; b, splenic infarct; c, splenomegaly lues; d, pancreatic cyst.

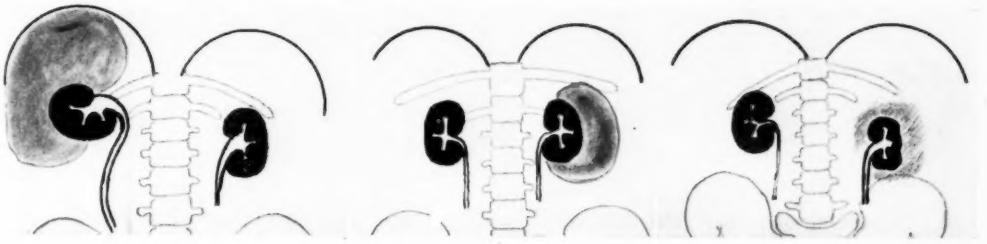
Subdiaphragmatic abscess. A subdiaphragmatic abscess, especially when large, will definitely displace the kidney downward and may also rotate it outward (Fig. 4).

Perinephritic abscess. There is no renal displacement in perinephritic abscess, no matter where the abscess is located. The kidney, however, will become permanently displaced and fixed in one position after the surgical drainage and the resulting inflammatory adhesions of the retroperitoneal space. It has lost its mobility and remains fixed in a mass of hard scar (Fig. 4).

Fig. 2d

a b c

Fig. 3. a, Retroperitoneal tumor; b, retroperitoneal infiltrating sarcoma; c, fibrosarcoma.



a b c

Fig. 4. a, Subdiaphragmatic abscess; b, perinephritic abscess; c, perinephritic fixation.

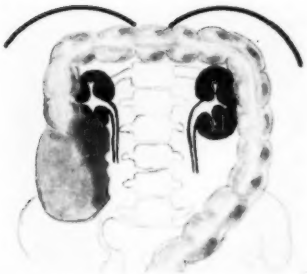


Fig. 5. Diverticulitis plus abscess of ascending colon.

Ascending and descending colon. The colon will not displace the kidney, no matter how much dilated it has become. Even massive carcinomatosis will remain without influence upon the kidney. In massive diverticulitis with large abscess formation, no renal displacement was noted (Fig. 5).

Adrenal. If the adrenal tumor is large it will invariably displace the kidney downward. The kidney remains uninfluenced by small tumors (Fig. 6).

Pelvic organs. There is no renal displacement by the massive growth of any of the pelvic organs. Large ovarian cysts or huge uteri in pregnancy do not displace the kidney (Fig. 6).

Spine. In scoliosis of the spine the kidney may be rotated and swung outward, and may be ptosed (Fig. 6).

SUMMARY

The kidney can be displaced by the spleen, retroperitoneal tumor, subdiaphragmatic abscess, the adrenal, the spine, and by perinephritic adhesions. It will not be displaced by the liver, perinephric abscess, ascending colon, descending colon, or pelvic organs.

DISPLACEMENT BY KIDNEY OF ADJACENT ORGANS

Liver. The liver is not displaced by any renal pathological process. It could only be affected by a tumor or cyst of the upper pole. Our studies of such films failed to show any displacement (Fig. 8).

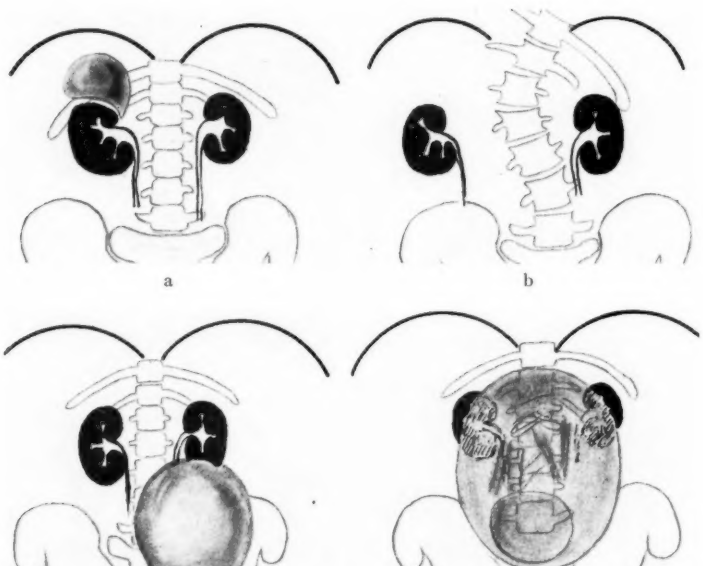
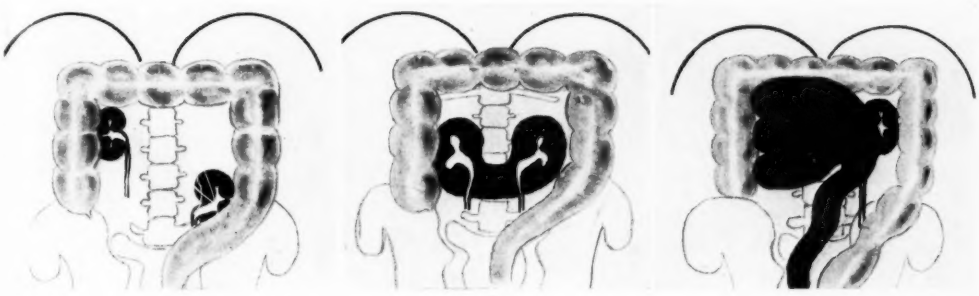
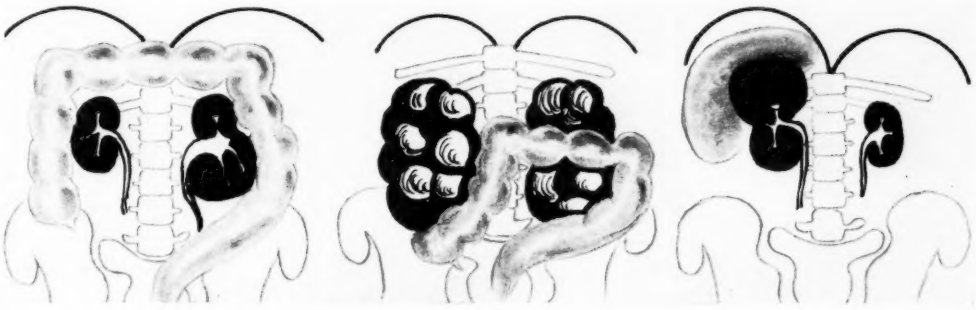


Fig. 6. a, Adrenal tumor; b, scoliosis; c, ovarian cyst; d, pregnancy.

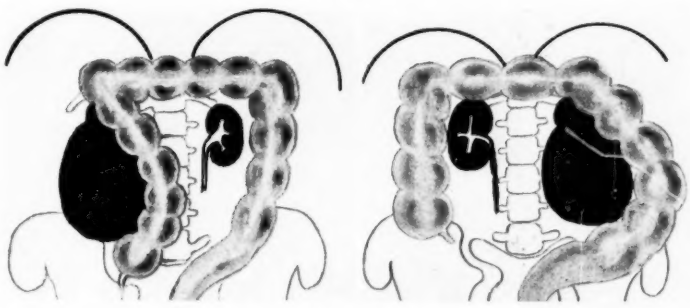


a b c

Fig. 7, a, Ptosis; b, horseshoe; c, hydronephrosis.



a b c



d e

Fig. 8. a, Tumor; b, polycystic kidneys; c, cyst of upper pole; d, cyst of right lower pole, e, cyst of left lower pole.

Spleen. The spleen is not displaced by the kidney in any pathological condition of tumor or cyst of its upper pole.

Ascending and descending colon. Both the ascending and descending colon are markedly displaced by bilateral polycystic kidneys. The ascending colon is pushed inward and forward, while the descending colon is displaced outward and forward. This has been observed in all cases with true polycystic disease. A tumor of the lower pole, either hypernephroma or cyst, will displace the ascending or descending colon depending upon which side is affected. The colon is not displaced in horseshoe kidney, in renal ptosis, nor in huge hydronephrosis (Figs. 7 and 8).

Adrenal. An upper polar tumor of the kidney will always displace the adrenal in its upward growth, pushing it inward.

SUMMARY

The kidney will displace the ascending and descending colon and the adrenals only. It will not displace the liver or spleen.

EVALUATION OF STUDY

This study brings out some very interesting points. It shows that while the spleen invariably displaces the kidney, the liver (an organ similarly situated and much bulkier) will not do it; while a subdiaphragmatic abscess will dislodge the kidney, a perinephric abscess will not. A true retroperitoneal tumor will always cause displacement. The kidney on the other hand can displace only the colon and adrenal, not the spleen nor liver.

Kidney not displaced by:	Kidney displaced by:
Liver	Spleen
Perinephric abscess	Perinephritic adhesions
Ascending colon	Subdiaphragmatic abscess
Descending colon	Adrenal
Pelvic organs	Spine
Kidney does displace:	**Kidney does not displace:**
Ascending colon	Liver
Descending colon	Spleen
Adrenal	

The facts brought out in this study are of value for the differential diagnosis of tumor masses in the abdomen by limiting the possibility of renal displacement to only a few instances.

We want to thank Drs. E. P. Pendergrass and P. Hodes for their co-operation.

EXPERIMENTAL STUDY OF THE SURGICAL TREATMENT OF CORONARY DISEASE

MERCIER FAUTEUX, M.D., F.R.C.S.(C), Montreal, Canada

CARDIAC surgery, proceeding carefully and methodically, has already accomplished much for the relief of coronary disease. The earliest operations were upon the sympathetic nervous system and were designed to relieve the pain of angina pectoris through interruption of the nervous pathways. Later attempts were made to increase the blood supply of ischemic myocardium by grafting onto the heart, from which it was hoped collateral circulation would be supplied. These operations, devised respectively by Beck and O'Shaughnessy, were based upon extensive experimental work and have already proved their value in human subjects.

The work of Leriche and his associates on vascular diseases of the extremities, especially partial arteriectomy, suggested one of the modes of attack here to be described. In their opinion the resection of a major arterial trunk gave on its most important objective the interruption of vasoconstrictive pathways. Their experimental studies and their results in human beings seem to substantiate that such a procedure almost invariably brings about vasodilatation and thus improves considerably the blood supply to the ischemic area. So impressed was Leriche with the beneficial and permanent results of partial arteriectomy in the extremities that he went so far as to suggest it as a worth-while procedure in coronary disease.

At the same time the value of venous ligation as an aid to the development of a collateral circulation has been emphasized by many workers. In 1913, Oppel demonstrated the efficacy of ligating the popliteal vein in the treatment of senile gangrene of the foot. In 6 cases thus treated the extremities recovered not only their warmth and color without the development of edema, but also a certain degree of hyperemia of the feet and toes. Four years later, as a result of the experimental work of Van Kend and the reports of Makins, Schrt, Propping, and Tuffier it could be stated as one of the fundamental principles in vascular surgery that the companion vein must always be ligated with the artery. This combined procedure according to Makins brings about its beneficial effect by maintaining within the limb for a longer period the smaller amount of blood supplied by the collateral arterial circulation. These findings were confirmed by Brooks and his co-workers and by Holman and his associates. Pearse, and Pearse and Morton have shown that this procedure realizes: (a) an increase in the residual arterial pressure; (b) an increase in the venous pressure; (c) an increase in minute flow from end of divided artery; (d) an increase in the peripheral arterial circulatory bed.

The following experiments were undertaken in order to observe the effect of these two procedures: (a) partial coronary resection and (b) partial coronary resection combined with ligation of the accompanying vein.

EXPERIMENTS

Group 1. Partial resection of the ramus descendens. Fifteen dogs were used in this series. Under positive pressure ether anesthesia, the heart was exposed and the pericardium opened. In each case the ramus descendens was isolated near its origin with the least possible trauma and from one to one and a half centimeters of its length resected. Great care was taken to avoid injuring any of the branches emerging from this main trunk. Immediately after the resection, 6 animals developed arrhythmias and died at once from ventricular fibrillation. Three more died within 2 to 3 hours, probably from the same cause. Of the 6 remaining, 2 lived for 24 hours, 3 for 48 hours, 1 lived for approximately a year and died with signs of cardiac

From the Department of Experimental Physiology, McGill University.

Read before the Canadian Medical Association, Montreal, June, 1939.

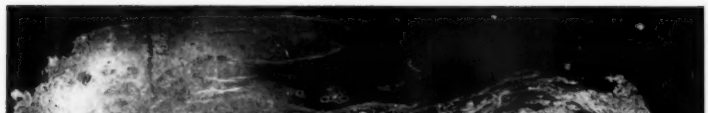


Fig. 1. The anterior half of a cross section of the heart at 4 centimeters from the lower end. At the lower left, part of the left wall; in the center, the septum; at the right, the wall of the right ventricle. The anterior part of the heart, lying over the septum and extending to the right and to the left, is made up of loose scar tissue covered with the two layers of the pericardium. At the upper left is part of the lung which is adherent to the heart.

failure. At the autopsy, it was found that the resection had been performed at a level much lower than in the other dogs (3 centimeters below the origin of the ramus descendens).

This group constitutes a control series, and the results are quite similar to those following ligation of the ramus descendens at the same level. Porter ligated this branch a few millimeters from its origin in 2 dogs; 1 died 4 days later, the other 14½ days later. Miller and Matthews stated that either main trunk of the left coronary artery may be ligated without seriously disturbing the heart provided the ligation is distal to the septal branch. Leriche, Hermann, and Fontaine concluded from their experiments that ligation of the ramus descendens above its important first collateral branches is always fatal. According to Wood, Clark, and Wolferth, ventricular fibrillation is the usual cause of death in coronary occlusion experiments. It occurs, as a rule, within 3 or 4 minutes whenever the left posterior circumflex artery is occluded; but more slowly after obstruction of the left anterior descending branch.

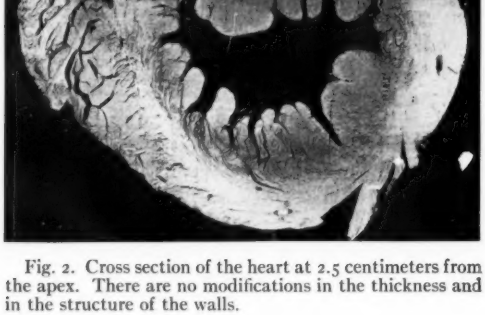


Fig. 2. Cross section of the heart at 2.5 centimeters from the apex. There are no modifications in the thickness and in the structure of the walls.

Group 2. Partial resection of the ramus descendens associated with ligation of the vena magna cordis. Fifty dogs were used in this series. Under positive pressure ether anesthesia, the pericardium was opened and the vena magna cordis was well exposed near the origin of the coronary sinus. Careful dissection of this vein is important because the proximity of the circumflex artery which lies closely beside it may result in its being included in the vein ligature. Such an accident is in most cases followed by ventricular fibrillation and death.

By means of a hook a thread was passed under the vein and the ligature was tied. This could be done without causing any bleeding and changes in the cardiac rhythm. Immediately after the ligation all the venous branches distal to the ligature dilated with blood and the anterior aspect of the heart took on a bluish color. The level of origin of the ramus descendens was then accurately localized and the trunk carefully dissected for a distance of 1 to 2 centimeters at the same

level as in the control animals of Group 1. All small branches emerging from it were first ligated and then arteriectomy, as in Group 1, was performed. In no case during this second stage were any changes observed in the cardiac rhythm. Immediately after the resection it could be seen that the arterial segment distal to the resection was not emptied but was as full of blood as if there had been no interruption in the continuity of the vessel.

Five dogs died from infection of the wound and pleural effusion; 2 from air embolus apparently caused by excessive intrapulmonary pressure at the moment of closing the pleura; 4 died a few months later from intestinal disorders. The 39 remaining lived and were kept under observation for more than a year and a half. During the whole of this time they apparently were in perfect health. (It is interesting to note that a few became pregnant and gave birth to puppies without showing any signs of cardiac disturbances.) They were then sacrificed. The studies of the hearts by injections, x-ray, and histological sections will be described in detail in a further report. It may be stated now from the preliminary histological studies that the myocardial lesions vary greatly; in some instances an infarct and subsequent scar formation occurs, in others there are, after 1 year, no apparent lesions in the myocardial structure (Fig. 2).[1]

Group 3. Ligation of the vena magna cordis vein followed a year later by partial resection of the ramus descendens. Ten dogs were used in this series. As all the experiments and results were essentially the same, only 1 will be described in detail.

Dog 51. On February 22, 1938, the vena magna cordis was ligated, and the postoperative course was uneventful. On March 7, 1939, partial resection of the ramus descendens was done. At this second operation the left lung appeared slightly adherent to the pericardium but was otherwise healthy. After careful liberation of this portion of the lung, the pericardium was incised. No fluid was present in the pericardial sac, and the few adhesions between the two surfaces of the pericardium did not seem to interfere with cardiac function. These adhesions were gently freed and the ramus descendens partially resected for 1.5 centimeters. The postoperative course was normal. On September 12, 1939, the dog was sacrificed. The ramus descendens was found to have been resected at 1 centimeter from the left coronary orifice. The coronary arteries were then injected with a barium mass. During this procedure it was noted that the injection mass penetrated the pulmonary fibrous tissue adherent over the pericardium by way of 3 small arterial vessels. This has been noted in other cases as well.

Histological report. The parietal pericardium is completely adherent to the anterior surface of the heart, the posterior surface being free. There is a scar on the anterior surface of the heart extending for 3 centimeters from the apex. This scar measures 1.5 centimeters in width. The ventricular wall at the level of the scar measures 3 millimeters in thickness. The most important lesion is the scar on the anterior aspect of the heart. This scar is formed of a connective vascular tissue showing still at the extreme periphery a few living muscle fibers. The Hiss bundle fibers in the region of the scar are healthy. It appears that this scar tissue is not truly scar tissue in the strict sense of the word. It does not appear as newly formed connective tissue.

It appears to be old connective vascular tissue deprived of its muscle fibers. The vessels, arteries, and veins are numerous and free from disease. There is no sclerosis or increased thickness of the arterial walls. At 2.5 centimeters from the apex, the most important branches of the ramus descendens are normal.

ANALYSIS OF STUDY

There is considerable evidence, both experimental and from necropsy observation, that the myocardial ischemia of coronary disease has as its chief danger the unbalanced distribution of the blood flow through the coronary arteries, rather than the decrease in the total blood volume to the muscle. When the heart succeeds, as it often does, in overcoming by itself the ill effects of coronary narrowing or occlusion, it is not so much through acquiring additional blood from collateral sources outside the heart as through a re-adjustment of its own coronary circulation. Therefore, any surgical procedure designed to correct this unbalanced flow would seem both logical and justified.

The results of the experiments in Group 1 show that in most cases partial arteriectomy alone was incompatible with life. One must not forget, however, that these experiments were performed on normal dogs with normal arteries and that resection under such conditions produces a disturbance of the coronary blood flow far different from that which results from

[1]The first experimental results were communicated to the Montreal Physiological Society, December 20, 1937.

gradually obliterating arterial disease in which the process is slow and in which the periarterial nervous pathways are not cut off.

It is suggested that if experiments could be conducted in such a manner as to reproduce fairly exactly the arterial conditions found in coronary thrombosis or occlusion, it might be possible to demonstrate that the diseased coronary artery, no longer a blood carrier, acts as a foreign body which gravely disturbs the coronary circulation by initiating vasospastic reflexes. Such experiments are actually in progress.

The experiments in Group 2 demonstrate that ligation of the vena magna cordis has a protective effect against the ventricular fibrillation which so often occurs in acute ischemic conditions and also minimizes the myocardial changes which follow occlusion or partial resection of the ramus descendens.

Furthermore, the experiments in Group 3 show that venous ligation has not merely a temporary value in improving coronary circulation; even a year after venous ligation, partial resection of the left ramus descendens, done at the same level as in Group 1, in which all the dogs died was not followed by death.

In 1937, Gross reported his attempts to increase the blood supply to the dog's heart by means of coronary sinus ligation. We have repeated these experiments in a series of 15 dogs. Either coronary sinus ligation was done or else partial obliteration by means of intrasinusal or perisinusal escharotic injections as proposed by him. Coronary sinus ligation gave us high mortality; and it is clear that occlusion of the venous drainage at such a high level is unnecessary to produce the desired effects. Injection of escharotics may be an advisable procedure in laboratory work but is dangerous in humans because of the necrosis which it sometimes produces in the right auricle and ventricle and of the serious inflammatory reactions which are set up in the pericardium.

Recently Gregg and Dewald performed experiments to study the immediate effects of coronary sinus and coronary vein occlusion on the coronary circulation. They found that the peripheral coronary backflow was markedly increased in the ramus descendens after acute coronary sinus ligation. The maximum retrograde flow was reached in from 10 to 30 minutes, and after sinus release did not immediately return to the control backflow figure. The blood was highly unsaturated, containing only 3 to 4 volumes per cent of oxygen. They concluded that sinus ligation does not prevent failure of contraction in a myocardial area from which the normal blood supply has been acutely removed and considered that such a procedure cannot be regarded as a method of choice for encouraging the blood supply to a potentially infarcted area.

These experiments varied in time from a few minutes to about 8 hours. Can one conclude from these results that if it should be possible to carry the same experiments for a longer period it may not show other facts demonstrating that venous ligation has a protective value in coronary occlusion or resection? The results reported in Group 2 and Group 3, when compared with those in Group 1, seem to justify a positive reply.

We do not yet understand exactly what are the circulatory mechanisms which are set up by venous ligation. It is probable that the blood reaching the distal end of the ramus descendens through branches of the right coronary artery, but chiefly from those of the circumflex artery, passes from them through the capillary bed of the ramus descendens, and, as the ligation of the vena magna cordis prevents its easy return to the coronary sinus, it forces a circulation through smaller vessels in the vicinity.

Most workers who have studied the effects of venous ligation in arterial occlusion in the extremities by experimental and clinical observation agree that in both veins and arteries distal to the level of obstruction there is an increase in the blood pressure, and that incidence of gangrene is diminished. Our experiments seem to confirm their general findings when applied to the coronary circulation. Small infarcts are found in some cases but they are completely absent in others.

SUMMARY AND CONCLUSIONS

It has been suggested that the similarity of arteriosclerotic disease of the coronary arteries

and of the extremities should permit of the application in the heart of surgical methods found useful in the treatment of peripheral vascular disease. Experiments on dogs are described in which were performed: (a) partial coronary arteriectomy of the ramus descendens; (b) partial coronary arteriectomy of the same arterial trunk combined with ligation of the vena magna cordis.

When partial resection of the ramus descendens at a high level was done a high mortality resulted. When the same procedure was carried out after venous ligation all dogs, apart from those dying of operative complications and intercurrent diseases, remained healthy for over a year.

It is concluded that vena magna cordis ligation in occlusion of the left ramus descendens helps to maintain adequate coronary circulation after partial coronary arteriectomy.

The results of these experiments suggest that in cases properly selected coronary vein ligation may be expected to act as a preventive measure against a second attack of coronary thrombosis and also to improve the coronary circulation sufficiently to relieve the pain of "angina of effort."

Furthermore it seems a logical procedure in traumatic surgery of the heart whenever it is necessary to ligate an important coronary arterial branch that is bleeding.

I wish to express my appreciation to Professor B. P. Babkin, professor of physiology, McGill University, for his constant interest and encouragement in this work, to Dr. C. S. Beck for important advice on the management of the heart surgically, to Dr. L. C. Simard for histological studies, to Dr. H. Mortimer for the x-ray work he so generously carried on, and to Dr. Melville for the electrocardiograms.

BIBLIOGRAPHY

1. Beck, C. S. A new blood supply to the heart by operation. Surg., Gynec. & Obst., 1935, 61: 407.
2. Idem. The development of a new blood supply to the heart by operation. Ann. Surg., 1935, 102: 801.
3. Idem. Further data on the establishment of a new blood supply to the heart by operation. J. Thoracic Surg., 1936, 5: 604.
4. Beck, C. S., and Tichy, V. L. The production of collateral circulation to the heart. Am. Heart J., 1935, 10: 849.
5. Blum, L., and Gross, L. The technique of experimental coronary ligation. J. Thoracic Surg., 1937, 5: 522.
6. Davies, D. T., Mansell, H. E., and O'Shaughnessy, L. Surgical treatment of angina pectoris and allied conditions. Lancet, 1938, 1: 1.
7. Fontaine, R. A propos du traitement des artérites oblitérantes par les résections artérielles. Bull. et mém. Soc. nat. de chir., 1931, 57: 1184.
8. Fontaine, R., and Schattner, R. Les bases expérimentales de l'artériectomie. J. Chir., Paris, 1935, 46: 849.
9. Gregg, D. E. Personal communication.
10. Gregg, D. E., and Dewald, D. Immediate effects of coronary sinus ligation on dynamics of coronary circulation. Proc. Exper. Biol. & Med., 1938, 39: 202.
11. Idem. Immediate effects of the occlusion of the coronary veins on collateral blood flow in the coronary arteries. Am. J. Physiol., 1938, 124: 435.
12. Gross, L., Blum, L., and Silverman, G. Experimental attempts to increase the blood supply to the dog's heart by means of coronary sinus occlusion. J. Exper. Med., 1937, 65: 91.
13. Leriche, R. Du syndrome sympathique consécutif à certaines oblitérations artérielles traumatiques. Bull. et mém. Soc. nat. de. chir., 1917.
14. Idem. Résultats éloignés des ligatures et des résections artérielles. Cong. de l'Ass. Franç. de Chir., 1922.
15. Idem. A propos de l'embolectomie et de l'artériectomie dans les thromboses oblitérantes. Bull. et mém. Soc. nat. de chir., 1931, 57: 524.
16. Idem. Considérations sur le traitement des artérites et des embolies artérielles, d'après une centaine de cas. Lyon méd., 1933, 151: 393.
17. Leriche, R., and Fontaine, R. Chirurgie des nerfs du coeur. Rap. au 41e. Cong. de Chir., 1932.
18. Idem. Conditions nécessaires, résultats et technique de l'artériectomie dans les oblitérations artérielles, d'après 80 opérations. Presse méd., 1935, 43: 1953.
19. Leriche, R., and Heitz, J. De la réaction vasodilatatrice consécutive à la résection d'un segment artériel oblitéré. Compt. rend. Soc. de Biol., 1917, 80: 160.
20. Leriche, R., Hermann, L., and Fontaine, R. Ligature de la coronaire gauche et fonction cardiaque. Compt. rend. Soc. de Biol., 1931, 107: 545.
21. Leriche, R., and Policard, A. Remarques cliniques sur les oblitérations artérielles localisées. Paris méd., 1921, 11: 27.
22. Makins, G. Hunterian Oration. Lancet, 1917, 1: 249.
23. Oppel, W. A. Wieting's Operation und der reduzierte Blutkreislauf. Wratschebnaja Gaz., 1913, 40: 1241.
24. O'Shaughnessy, L. Surgical treatment of cardiac ischemia. Lancet, 1934, 1: 185.
25. Idem. An experimental method of providing a collateral circulation to the heart. Brit. J. Surg., 1936, 23: 665.
26. Propping, K. Ueber die Ursache der Gangran nach Unterbindung grosser Arterien. Muenchen. med. Wchnschr., 1917, 66: 596.
27. Schrt, E. Ueber die kuenstliche Blutleere von Gliedmassen und unterer Koerperhaelfte sowie ueber die Ursache der Gangran des Gliedes nach Unterbindung der Arterie allein. Med. Klin., 1916, 12: 1338.
28. Stricker, P. Des résections artérielles étendues dans le traitement de certaines artérites oblitérantes. Rev. de Chir., Paris, 1928, 66: 214.
29. Stricker, P., and Orban, F. Recherches expérimentales sur la thrombose artérielle, les artérites, la gangrène et sur la valeur comparée des ligatures artérielles et des artériectomies. J. Chir., 1930, 36: 687.
30. Van Kend. Compt. rend., Conf. Interall. Paris, 1917, 348.
31. Wood, F., Clark, and Wolferth. Experimental coronary occlusion. Arch. Int. Med., 1933, 51: 771.

CARBOHYDRATE METABOLISM IN THYROTOXICOSIS

I. An Experimental Study

E. E. BLANCK, M.D., Chicago, Illinois

THE relation of the thyroid secretion to metabolism is a problem that has attracted considerable interest. Though a voluminous literature attests the painstaking clinical and experimental studies that have been made, many of the ties in this relationship remain poorly understood.

REVIEW OF LITERATURE

The early fund of knowledge—that is prior to 1900—was based almost entirely on clinical observations. It was observed that an increased thyroid secretion was associated with an increase, and the hypothyroid state with a decrease, in both the total and protein metabolism. In addition there was known to exist some derangement in the metabolism of carbohydrate, for it was noted that the exophthalmic goiter syndrome was sometimes associated with a persistent or transient glycosuria. Further, in some obese or myxedematous individuals, glycosuria followed the administration of thyroid extract only to disappear when the extract was discontinued. The interpretation of these observations was that hyperthyroidism was associated with a decreased glucose tolerance. Magnus-Levy and Garrod gave accounts of this literature.

With the turn of the century, experimental study began to supplement clinical investigation. Eppinger, Falta, and Rudinger studied the relationship between the thyroid gland and the metabolism of carbohydrate. They reported that epinephrine injected into thyroidectomized dogs failed to produce the glycosuria that occurred in normal animals. From the precedent of studying these changes in the thyroidectomized animal, conflicting reports appeared in the literature. Most workers continued to agree that an excess thyroid secretion augmented both the total and nitrogen metabolism, but an uncertainty arose as to the effect on the metabolism of carbohydrate. Opinion became divided as to whether the thyroidectomized animal possessed an increased or decreased tolerance for glucose. This uncertainty was due to the fact that most studies were made on thyroidectomized dogs. Because of the close anatomical relationship of the thyroid gland and parathyroid glands in this animal, it was difficult to recognize the separate effects of thyroidectomy and parathyroidectomy. Reviews of this literature were given by Cramer and Krause (7) and Kuriyama.

As additional studies were made to clarify this controversy, another thought was introduced into the experimental studies of hyperthyroidism. The effect of feeding thyroid to the normal animal was coming under consideration. Carlson and his co-workers in a series of observations found that desiccated thyroid given by mouth is toxic for many animals and that different genera exhibit great variation in their susceptibility. Dogs, cats, foxes, and ducks were most resistant; rodents and primates the least. French confirmed the toxicity of thyroid for rabbits, rats, and guinea pigs. Control animals fed with other organs or tissues failed to reveal evidence of toxicity.

At this time Cramer and his associates started a series of investigations into the effect of thyroid feeding on metabolism. Because of the far-reaching influence of their communications the salient features are recalled in a brief summary. In a preliminary report, Krause and Cramer (26) reported a lowering for the limit of assimilation of glucose in thyroid-fed dogs. In their next paper (7), they reported that after feeding thyroid for 2 or 3 days to rats and cats, there was a complete loss of liver glycogen. Since the animals were fed a carbohydrate-rich diet and no reducing sugar was found in the urine, the

From the Division of Surgery, Northwestern University Medical School.

interpretation was that the thyroid hormone acted specifically on only one phase of carbohydrate metabolism, and that was to inhibit the formation and storage of glycogen in the liver. After a lapse of 4 years, Cramer and McCall (8, 9, 10, 11) renewed the studies to investigate the gaseous metabolism of thyroidectomized and thyroid-fed rats. Each communication added new factors to account for the deranged metabolism of carbohydrate. Their final interpretation was as follows: In thyroid-fed animals the liver formed glycogen all the time. But the excess thyroid hormone stimulated the suprarenal glands to greater activity and this increased the mobilization of hepatic glycogen. The organism responded to this carbohydrate plethora by increasing the oxidation of carbohydrate. When the glycogen reserve was depleted, the preformed carbohydrate of the diet was inadequate to meet the increased demand for carbohydrate and there was a breaking down of body fat and protein to form carbohydrate for oxidation. On this basis it was suggested that the hyperthyroid patient be fed a diet rich in carbohydrate "to counteract the loss of flesh."

The studies by Cramer and his associates exerted considerable influence in shifting interest from the altered fat and protein metabolism to that of the deranged metabolism of carbohydrate. To facilitate a review of the inquiries into the deranged metabolism of carbohydrate, the key references are divided into one of three groups. One group investigated the changes in blood and urinary sugar. The second studied the utilization of glucose as influenced by an excess thyroid secretion, whereas the third investigated the rôle played by the liver in hyperthyroidism.

The change of interest in this interval was further facilitated by standardization of methods for the determination of blood sugar. With this standardization a number of workers studied changes in the blood and urinary sugar, before and after the administration of glucose. Contributions to this subject by Geylin and others (12, 18, 21, 30) served to establish a number of observations. Neither a fasting hyperglycemia nor a spontaneous glycosuria was of constant occurrence in hyperthyroidism, but after a glucose test meal there was an alimentary hyperglycemia. Associated with the administration of glucose, sugar was usually spilled in the urine. With the clinical improvement that followed rest or operation, there was a reduction in the hyperglycemia and glycosuria. No relationship was demonstrated between the severity of intoxication and degree of impaired tolerance.

Another demonstration of this impaired tolerance was made by Wilder and Sansum (36). In a clinical study of glucose tolerance they employed the continuous, timed, intravenous injection of glucose. Their observations were made in normal human individuals and in a series of pathological conditions, of interest being the 5 patients with exophthalmic goiter. In the normal individuals glucose was injected up to a rate of 0.85 gram per kilogram body weight per hour without producing glycosuria. But in the patients with exophthalmic goiter, sugar appeared in the urine with slower rates of injection ranging from 0.5 to 0.65 grams glucose per kilogram body weight per hour. From these findings they concluded that patients with an increased thyroid function uniformly showed a diminished rate of tolerance for the intravenous administration of glucose.

This syndrome of a decreased tolerance for glucose suggested that the altered carbohydrate metabolism of thyrotoxicosis may be analogous to the derangement observed in diabetes mellitus. John (22, 23, 24) and Wilder (35) reviewed this literature and made an extensive clinical study of this relationship. They demonstrated that hyperthyroidism does not act as an exciting etiological factor of diabetes mellitus but that it might fan a latent diabetes into activity or intensify a diabetes already present. The clinical importance in this relationship was that the exophthalmic goiter syndrome reduced the ability of the diabetic patient to utilize carbohydrate, decreased the efficiency of the unit of insulin, and increased the danger of sudden onset of diabetic coma. Control of the hyperthyroidism by rest, administration of iodine, and operation greatly improved the diabetic patient's tolerance for carbohydrate.

These inquiries led to the second group of studies, namely, the investigation of glucose

utilization in hyperthyroidism. This included both clinical and experimental investigations. DuBois in direct calorimetric studies of patients with exophthalmic goiter demonstrated that there was no interference with the oxidation of carbohydrate. Sanger and Hun studied changes in the blood sugar and respiratory quotient, before and after the administration of glucose. They concluded that individuals with thyrotoxicosis burned carbohydrate readily, but that the liver was unable to store glycogen. Mirsky and Broh-Kahn made direct observation on the utilization of carbohydrate in experimental hyperthyroidism. They studied the rate at which glucose disappeared from the blood of eviscerated rabbits. In the control rabbits the average disappearance in 1 hour was 35.6 per cent. In the hyperthyroid rabbits the average disappearance in 1 hour increased to 75.6 per cent, demonstrating that the extrahepatic tissues of the hyperthyroid animal removed glucose from the blood at a greater rate than did those of the normal animal. Since the liver was not present to influence the blood sugar, the increased utilization of glucose by the extrahepatic tissues was not secondary to any defect in the glycogenic or glycogenolytic mechanism of the liver.

In the third and last major group of communications, interest was centered on the rôle played by the liver. This group, more than the others, gave rise to considerable confusion. Most of the studies followed the report by Cramer and Krause that thyroid feeding depleted the liver of its glycogen reserve. As pointed out before, Cramer and Krause in their initial studies, believed that in hyperthyroidism, the liver was unable to form or store glycogen. On this basis there followed in the past two decades a stream of experimental studies designed to demonstrate in one fashion or another that thyroid feeding depleted the liver of its glycogen reserve. Confronting this group, a number of clinical observations suggested that the liver was not primarily responsible for the altered metabolism of carbohydrate. Richardson, Levine and DuBois studied the curves of the respiratory exchange in a normal individual and in 2 cases of exophthalmic goiter. They concluded that there was no defect in the mechanism by which glycogen was stored and estimated that the glycogen reserves were as large in the 2 patients with exophthalmic goiter as in the normal subject. Later, Johnston made a similar study in children with exophthalmic goiter and demonstrated that there was no impairment in the oxidation of carbohydrate. He also pointed out that when the glycogen stores were well maintained through rest and diet, injected glucose was oxidized more readily in the patients with exophthalmic goiter than in normal individuals. Two schools of thought developed from these conflicting reports. One, based on experimental studies, contended that the liver in hyperthyroidism was unable to form and store glycogen. The other, based on indirect clinical observations, maintained that the liver did form and store glycogen.

To help clarify this controversy a smaller but no less significant group of studies gave some aid to this problem. Burn and Marks (1, 29) studied the function of the liver as it contributed to maintain a constant blood sugar level. In their thyroid-fed animals they found the liver more responsive to the stimuli that promoted glycogenolysis. The result was a ready release of stored glycogen. Similarly, John quoted the studies of Charvát and Gjurič (3, 4) who demonstrated that in exophthalmic goiter the glycogen poor liver was in a state of shock and that it not only bound glycogen loosely but released it readily.

STATEMENT OF PROBLEM

In the review of the literature, the purpose was to follow the progress in our understanding of how an excess of the thyroid secretion influences metabolism. It was pointed out that by the latter years of the nineteenth century, clinical study had shown that an increased thyroid secretion was associated with some derangement in the metabolism of carbohydrate. Then with the turn of the century experimental work demonstrated that thyroid feeding depleted the liver of its glycogen reserve. This stimulated a long train of both experimental and clinical investigations. It was first demonstrated that hyperthyroidism was associated with a decreased

tolerance for glucose. Since the decreased tolerance observed in hyperthyroidism resembled the impairment in diabetes mellitus, it appeared that a relationship might exist between these entities. Although further study failed to demonstrate any direct relationship between hyperthyroidism and diabetes mellitus, it led to the investigation of glucose utilization in hyperthyroidism. This latter investigation demonstrated that the extrahepatic tissues of hyperthyroidism burned glucose with avidity. Paralleling these studies other workers tried to correlate these observations with the impoverishment that occurred in the hepatic store of glycogen. Some insight was given by demonstrating that the hyperthyrotic liver bound glycogen loosely and released it readily, but a fundamental problem was still concerned with what rôle the hyperthyrotic liver played in this deranged metabolism of carbohydrate.

MATERIALS AND METHODS

Male albino rabbits—species of New Zealand white—were used exclusively in this study. All animals were of the same colony completing their active growth at 9 months with a body weight of 3.0 to 3.2 kilograms. The rabbits were a "small breed" of New Zealand white. In accordance with the precedent set by the literature the animals were selected for study when they attained a weight of 2.7 kilograms (approximately 6 pounds). At this weight the rabbits were from 7 to 8 months of age and had completed their active growth. The animals were housed in regulation-size hutches and gentled throughout the periods of observation. Twice daily they were fed weighed portions of a commercial combined ration (Victoria rabbit feed). Fresh water was supplied *ad libitum*. Each morning when the animals were weighed any food that remained was again weighed to determine the intake for the preceding day. After an adequate control period, thyroid was given orally and the dose controlled by mixing pulverized desiccated thyroid tablets with each feeding.

For comparison and control on the changes in weight a litter of 7 rabbits was reared for a period of 1 year. Food was supplied *ad libitum* and each animal was weighed every second day. This formed the basis for the normal growth curve representative for this colony. Unfortunately, at the time of this study the significance of determining the normal food intake (to supplement normal growth curve) was not appreciated; so data on the normal food consumption are in part lacking.

The glycogen content of the liver was determined in both normal and thyroid-fed animals. In the early periods of study a surprising lability was noted in the glycogen stores of the liver. Because of this lability, study of the normal rabbits was not designed to effect the conventional uniformity. Instead, the animals were studied only after quantitative changes were made in the diet. The purpose was to note the latitude of glycogen storage in normal animals. In the thyroid-fed animals a standardized method of study was developed. When an experiment was interrupted in the terminal stage of thyroid feeding the hepatic store of glycogen was exhausted. Since an attempt was made to correlate the status of the glycogen deposit in the liver with other observations, the plan was altered to interrupt each experiment before the onset of the terminal stage. With this modification titratable quantities of glycogen were present, and it is on this basis that the animals in this paper were studied. Food was withdrawn the night before so that an 8 hour fast preceded the removal of samples from the liver. Following the precedent of other writings the glycogen determinations were made in duplicate. In the first experiments, samples of liver were removed after the animal was stunned by a sharp blow over the occiput. But after the studies were in progress it was learned from a paper by Cori that with stunning of an animal the profound discharge of nervous impulses might alter the glycogen content of the liver. The method was then changed first to anesthetize each animal with the intravenous administration of sodium pentobarbitol. The subsequent procedure was carried out according to Sahuyn's modification (33) of Pflueger's method for the determination of glycogen. The sugar content of the hydrolyzed samples was determined by the standard method of Folin and Wu.

EXPERIMENTS AND OBSERVATIONS

Influenced by the literature, this study of a deranged carbohydrate metabolism began by investigating the glucose tolerance curve of thyroid-fed rabbits. Following the precedent set by other workers, rabbits were fed 5 grains of desiccated thyroid daily and the glucose tolerance curve studied after varying periods of thyroid administration. The results were similar to the observations made by Burn and Marks in that the character of the glucose tolerance curve varied with the duration of thyroid feeding. As outlined herein, Burn and Marks explained these variations on the basis of the sugar-regulating mechanism of the liver.

While a study of the changes in the glucose tolerance curve was being made there was noted a loss of appetite following the institution of thyroid feeding. Since hyperthyroidism was reputed as having associated with it not only an increased but an almost voracious appetite, this observation was confusing. The first reaction was that the appetite loss was due to some error or unusual circumstance in the method of study. But with repeated experiments a loss of appetite frequently followed the administration of thyroid. It then appeared that thyroid substance, an animal protein and foreign to the natural diet of a rabbit, might be responsible for this anorexia. To test this possibility a number of changes were made in the routine of feeding. When an animal refused the feeding ration mixed with thyroid, the mixture was withdrawn and replaced by a fresh supply of the ration. Almost invariably the animal would refuse the new feeding. Since they now refused the ration they ate readily under normal conditions, it appeared that the presence of thyroid powder in the ration was not objectionable. For another test, animals were selected that had refused both the plain and thyroid-mixed feedings. They were tempted with tastier morsels as carrots, fresh lettuce, and greens. When an item was found that the rabbit would eat, it was sprinkled with thyroid powder and again offered. A refusal of these items could not be effected by the addition of thyroid powder, and from this it was concluded that the presence of thyroid powder in the ration was not responsible for the loss of appetite.

At this point it was thought that if the amount of thyroid was increased, the disproportion between the augmented metabolism and the amount of food taken would be so great that the animal might develop an increased or voracious appetite. Accordingly, additional series of rabbits were fed first 7.5 then 10, and finally 15 grains of desiccated thyroid daily. The results were the same, for even with the extreme intoxication effected by the massive doses of 15 grains daily—the appetite remained poor.

It was during the feeding of these larger doses that the appetite loss was demonstrated impressibly, through an accident. Two male rabbits, identical litter mates, were housed in adjacent hutches. It was planned to feed one rabbit 10 grains of thyroid daily and the other was to serve as a control. But after the second day of thyroid feeding it was noted that the control animal had an almost complete loss of appetite and was steadily losing weight. Because of the identical appearance of the animals it required several days to learn that through an accident the control animal had eaten the thyroid-food mixture. By this time the animals were lost to the proposed plan of study. That some value might be derived from this incident the feeding of thyroid was discontinued but observations on the changes in weight and food consumption were continued. The effects of this single massive dose of thyroid are illustrated in Chart 1.

As the duration for each experiment was extended and an increasing number of animals was studied, the changes in appetite associated with the prolonged administration of thyroid conformed to a definite pattern. A graphic illustration of this pattern based on the data of 3 rabbits receiving 7.5 grains of desiccated thyroid daily is given in Chart 2. The pattern consisted of four phases or periods. In the first few days there was no change in the amount of food normally taken. Following this latent period, the first effect of thyroid feeding was signalled by a loss of appetite. The extent of this anorexia was variable. In some animals there was a prompt and complete loss of appetite. In others the loss of

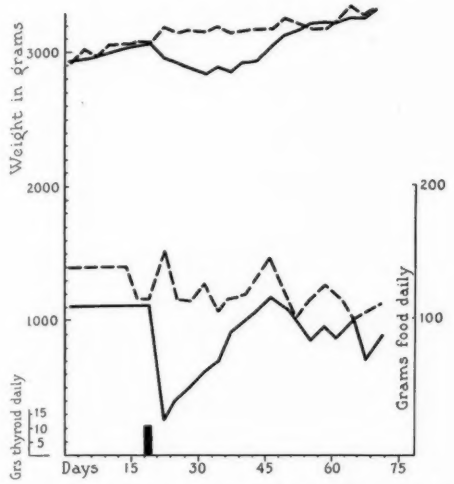


Chart 1. Illustrating the effects of a single massive dose of thyroid (20 grains in 24 hours). Solid lines represent thyroid-fed rabbit; broken lines, the normal control. The sudden loss of appetite and weight loss following thyroid feeding was well defined. As the effect of thyroid was spent the appetite improved and there was a corresponding gain in weight.

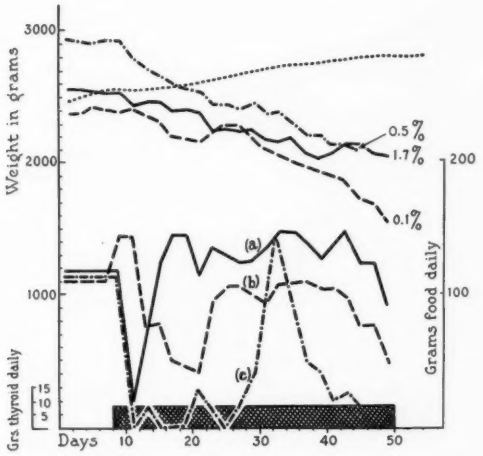


Chart 2. A comparative illustration of the appetite changes associated with the prolonged feeding of 7½ grains of thyroid daily. All 3 rabbits illustrate the sudden loss of appetite that immediately follows the institution of thyroid feeding. Subsequently, the appetite in rabbit A improved to exceed the normal intake. In rabbit B the improvement fell short of the normal level. In rabbit C the appetite failed to recover from its initial loss and continued at a low ebb for the duration of the experiment. The effect of the appetite on the weight curve and hepatic store of glycogen is also illustrated. The number at the end of each weight curve gives the average liver glycogen in milligrams per cent. The dotted line represents the normal growth curve for this colony.

appetite was less marked and developed gradually. Paralleling the diminished intake of food was a corresponding loss in weight. With the continued administration of thyroid the animal entered a second period of improvement. In the second period the appetite improved and there was a corresponding gain in weight. But these changes were also variable. Rarely did the appetite improve to exceed the normal intake. More often the improved appetite approached, but fell short, of the normal level. In still others the appetite showed no improvement and lagged at a low ebb for the remainder of the experiment. The maximal improvement attained in the second period marked the beginning of the third period. In contradistinction to the short, fulminating, preliminary phases, the third period was of longer duration and quiet. The appetite continued on its improved level with but minor fluctuations but the weight curve took on a gradual decline. After a long period the third phase gradually merged into the brief fourth period. The last period began with a fall in the appetite from its sustained level. There was a corresponding loss in weight and the animal began to manifest a growing weakness. As the last period progressed it gained momentum and in the brief anticlimax there was a complete abstinence from food with a precipitous fall in weight. A marked asthenia developed and with complete exhaustion the animal died. The last period was also variable. In some animals the fatal end approached rapidly, in others, the final succession of events was prolonged.

As the changes in appetite were formulating this pattern, the glycogen content of the liver was determined at the end of each experiment. Five normal and sixteen thyroid-fed rabbits were studied. The thyroid-fed rabbits were divided into four series. This division was based on the amount of thyroid fed each animal. Each series was further subdivided into pairs, as determined by the amount of food taken during the period of thyroid feed-

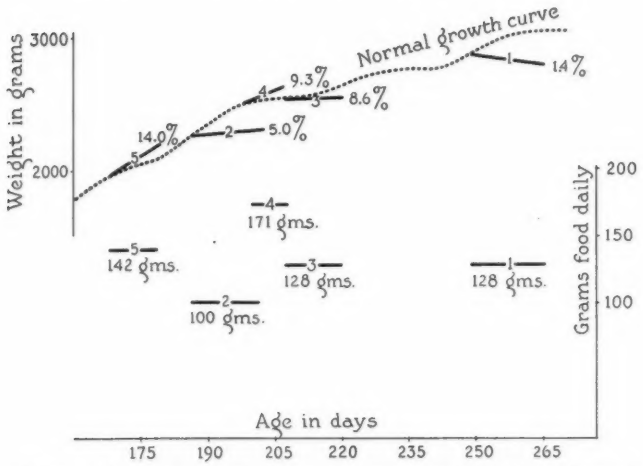


Chart 3. A comparative illustration of the changes in weight and hepatic store of glycogen in normal rabbits following quantitative changes in the diet.

ing. The changes observed are graphically illustrated in Charts 3, 4, 5, 6, and 7. In these charts the solid lines represent animals with the better appetites, the broken lines those with poorer appetites. The figure at the end of each weight curve is the average value for liver glycogen in milligrams per cent.

As indicated under materials and methods, the control animals were not studied to effect the conventional uniformity. Instead they were sacrificed only after quantitative changes were made in the diet. The purpose was to note to what extent the normal hepatic store of glycogen was influenced by quantitative changes in the diet. This in turn, was to aid the understanding of changes that occurred in the hepatic stores of glycogen under the influence of thyroid feeding. The results of the control experiments are illustrated in Chart 3.

In the control animals the influence of the appetite level on the quantitative store of glycogen was better appreciated when the corresponding weight curve of the animal was taken into consideration. This is best illustrated in rabbits 1 and 3. The appetite level was the same in both rabbits. But in the smaller animal, rabbit 3, the diet was sufficient to effect a normal weight gain, whereas the larger animal, rabbit 1, actually lost weight. The combination of these changes was reflected in the quantity of glycogen stored in the liver.

In the thyroid-fed animals, three factors were noted in studying the glycogen content of the liver. First, the hepatic store of glycogen was depleted only in the terminal period of thyroid feeding, and that was when the animal was moribund. When an experiment was interrupted before the terminal period a definite store of glycogen was present, even though the animal received thyroid for a long period. This was important, for it indicated that the liver formed and stored glycogen. Second, the animals that maintained higher appetite levels had the larger stores of glycogen. Since the liver that received the more abundant supply of materials from which to store glycogen was the liver that had the larger store of glycogen indicated again that the liver formed and stored glycogen. The third factor, and that was the daily dose of thyroid, also had a direct influence on the quantitative store of glycogen. The animals fed small doses of thyroid had larger stores of glycogen, demonstrating that the degree of intoxication had a direct influence on the quantity of glycogen stored in the liver. This was true for all animals except those receiving

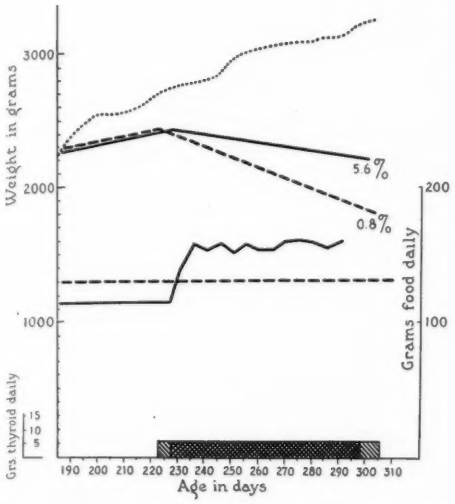


Chart 4. Illustrating the changes in weight and appetite associated with the prolonged administration of 5 grains desiccated thyroid daily. Solid lines represent animals with the better appetites, broken lines those with poorer appetites. The numbers at the end of each weight curve give the average liver glycogen in milligrams per cent. The dotted line represents the normal growth curve for this colony.

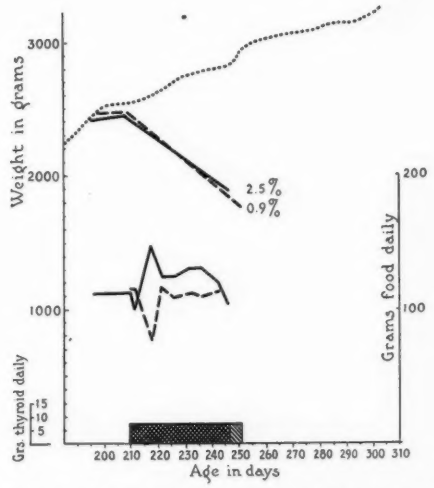


Chart 5. Illustrating the changes in weight and appetite associated with the prolonged administration of 7½ grains desiccated thyroid daily. Solid lines represent animals with the better appetites; broken lines those with poorer appetites. The numbers at the end of each weight curve give the average liver glycogen in milligrams per cent. The dotted line represents the normal growth curve for the colony.

7.5 grains daily. In this series the glycogen content was too small to correspond with the regular decline that followed the larger doses of thyroid. There were two reasons for this discrepancy. One was that the feeding of thyroid was unintentionally prolonged in this series to almost the terminal period. As a result the hepatic store of glycogen was reduced to a minimum and this reduced the average for the series. The other reason was that the two rabbits in this series having the best appetites, in reality, ate only fairly well as compared to similar animals in the other series. The findings for the thyroid-fed animals are illustrated in Charts 4, 5, 6, and 7.

Since the appetite level and degree of intoxication had a direct influence on the hepatic store of glycogen there remained to consider the element of time. The duration of thyroid feeding did not influence directly the quantitative store of glycogen. The only relationship was relative, for a lessening in the store of glycogen was associated with the early or final period of thyroid feeding. This demonstrated again that with long periods of thyroid feeding the liver still formed and stored glycogen.

When it was evident that glycogen was formed and stored in the liver and that the appetite level influenced the quantity of glycogen stored, the reaction was to have the animals eat more. Any measure that would increase the hepatic store of glycogen would be of therapeutic value and would prepare for a better understanding in the relation of the thyroid secretion to metabolism. Since the ration used was satisfactory, it was evident that more than an ample supply of food was needed. At first the rabbits were urged with alfalfa hay, lettuce, carrots, cabbage, and other items, but these were refused. Since the normal desire to eat was lacking, it was thought to create a false appetite with the injection of insulin. The initial doses were small and ineffective. Subsequently, the amount of insulin was increased until some animals were receiving 100 units of protamine-zinc insulin daily—but to no avail. Vitamin

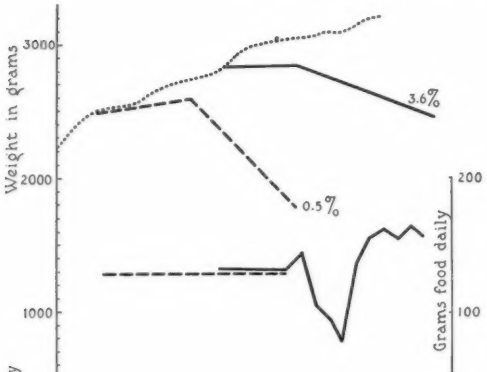


Chart 6. Illustrating the changes in weight and appetite associated with the prolonged administration of 10 grains desiccated thyroid daily. Solid lines represent animals with the better appetites; broken lines those with poorer appetites. The numbers at the end of each weight curve give the average liver glycogen in milligrams per cent. The dotted line represents the normal growth curve for this colony.

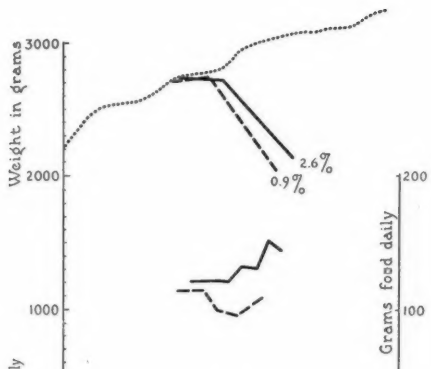


Chart 7. Illustrating the changes in weight and appetite associated with the prolonged administration of 15 grains desiccated thyroid daily. Solid lines represent animals with the better appetites; broken lines, those with poorer appetites. The numbers at the end of each weight curve give the average liver glycogen in milligrams per cent. The dotted line represents the normal growth curve for this colony.

B_1 was also tried. A slight improvement was noted when vitamin B_1 supplemented the ration but with the conditions that governed these experiments the results were negligible. Finally, it was concluded that the appetite could not be stimulated to a satisfactory level.

One of the most important factors in this study was the evidence indicating that in hyperthyroidism the liver formed and stored glycogen. Because the evidence supporting this contention was based on indirect observations it was felt necessary to offer more conclusive evidence in the form of direct observations. This motivated an investigation of the glycogen content of the liver in normal and thyroid-fed animals, before and after the intravenous administration of glucose.

MATERIALS AND METHODS

The principle was to determine the glycogen content of the liver before and after the intravenous administration of glucose. Full grown, male, rabbits, of the same colony, were used for these experiments. After a suitable control period, hyperthyroidism was produced by the oral administration of 7.5 grains desiccated thyroid daily. Food and water was supplied *ad libitum*. The animals were housed and cared for as detailed before.

Two normal and 5 thyroid-fed animals were studied. The thyroid-fed animals were selected for study when a definite hyperthyroidism was evident. The shortest period of thyroid feeding was 27 days, the longest period 53 days with an average duration of 42 days. Food was withdrawn the night before so that an 8 hour fast preceded the time of study. The following morning light anesthesia was effected by the intravenous injection of sodium phenobarbitol. Sodium phenobarbitol was chosen because the action is of longer duration than is that of other barbiturates and also because the anesthesia effected by it is reputed not to interfere with the formation and storage of glycogen in the liver. The abdominal wall was prepared aseptically and all procedures were carried out under aseptic conditions. The proposed line of incision in the right upper quadrant was infiltrated with a one-half per cent solution of novocain without epinephrine. This insured against any reaction by the animal. The peritoneal cavity was entered through a small incision. The presenting edge of liver was gently mobilized and a narrow strip of hepatic tissue, about 1 by 6 centimeters, was excised from the peripheral margin. The strip of tissue was quickly divided into samples and transferred into weighed tubes of hot potassium hydroxide. There was little bleeding from the cut edge. When hemostasis was needed sutures of fine silk

were carefully tied over the cut edge. As an added precaution a slip of omentum was incorporated under the ligatures. The abdominal wall was closed in layers. The external jugular vein on one side was exposed, cannulated, the time noted, and the intravenous administration of 5 per cent glucose in normal saline begun. To insure an ample supply of glucose, the solution was administered at a rate calculated to supply 0.8 to 0.9 grams glucose per kilogram body weight per hour. After an average of 4.5 hours of venoclysis preparations were made to conclude the experiment. The abdominal wall was again infiltrated with plain novocain and the peritoneal cavity was opened. Following a brief inspection to make certain there was no bleeding in the interim, a lobe of liver (other than the one selected for the first biopsy) was mobilized and a section of hepatic tissue was excised. The section of liver was cut into samples. Each sample was gently but quickly blotted on a soft cloth to absorb any excess glucose laden blood, and transferred to weighed tubes of hot potassium hydroxide. The urine in the bladder was removed for the quantitative determination of glucose, and the animal sacrificed.

The glycogen determinations were made after Sahuyn's modification of Pflueger's method. The sugar content of hydrolyzed samples was determined by the standard method of Folin and Wu. The first determinations were made in duplicate but when the wide variation between samples was noted, a larger number of samples was taken.

As just given, the rate of glucose administration was calculated to make available an ample but not exorbitant supply of glucose. This was reasonably successful for a definite but small quantity of glucose spilled into the urine of each rabbit. The direct observations made in these experiments demonstrated that the liver in hyperthyroidism formed and stored glycogen. The results for each rabbit are graphically illustrated in Chart 8. In the control rabbits the average store of hepatic glycogen increased from 1.7 per cent to 4.2 per cent after an average of 4¼ hours of glucose venoclysis. In the thyroid-fed rabbits the average store of glycogen increased from 1.0 per cent to 5.2 per cent after an average of 4¾ hours of glucose venoclysis.

RESULTS OF STUDY

The experiments in this study demonstrated first, the changes in appetite associated with the prolonged administration of thyroid and second, that glycogen was formed and stored by the liver in hyperthyroidism.

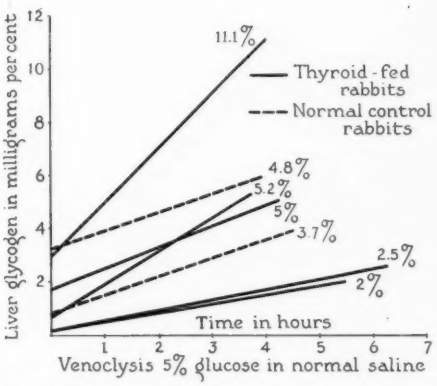


Chart 8. A comparative illustration of the changes in hepatic glycogen following the intravenous administration of glucose. Solid lines represent the storage of hepatic glycogen in thyroid-fed rabbits; the broken lines, the storage in normal rabbits.

The changes in appetite conformed to a pattern of four periods. Further, when each experiment was concluded and the appetite pattern viewed in its entirety, it was found that the animals frequently ate less during the period of thyroid administration than under normal conditions. But this varied. Some animals maintained appetites less than normal, others maintained normal appetites, and still others maintained appetites that surpassed the normal intake. Of more significance, however, was the fact that the appetite was never sufficient permanently to counterbalance the augmented metabolism.

When the diminished appetite was established by this study, confirmation of this observation was looked for in the literature. In other communications on experimental hyperthyroidism the loss of appetite was occasionally mentioned, but no significance was credited this observation. The explanation for this undoubtedly lies in the stereotyped experiment that was used. The experiments were incomplete from the standpoint of time and too fulminating to delineate the series of changes taking place. Consequently, the recognition of this appetite pattern was held in abeyance. On the clinical side a similar problem was found. A decreased appetite in clinical hyperthyroidism was mentioned on occasions, but in no instance was the signifi-

TABLE I.—APPETITE CHANGES IN CLINICAL HYPERTHYROIDISM

Number of cases	Relative change in appetite	Duration of symptoms in months	Average B.M.R. before iodine	Weight loss		Age
				pounds	months	
43	Less than Normal	15	40	20	16	49
30	Normal	28	44	11	14	41
27	More than Normal	41	42	19	21	40

cance of this observation recognized. The only exception was a recent communication by Frazier and Ravdin in which the authors reported a decreased appetite in some of their thyrotoxic patients and interpreted this change as a significant part of the general picture of thyrotoxicosis.

Since a loss of appetite was commonly associated with the administration of thyroid and only meager evidence to support this observation was found in the literature, inquiries were made into the appetite level of thyrotoxic patients on the service of Dr. Richter. Individuals with a definite thyrotoxicosis that had not received iodine or medical management were carefully questioned as to the status of the appetite. The purpose was to determine if the patient ate less than normal, normally, or if the appetite was increased to more than the normal level. On this basis one hundred patients were interviewed. Forty-three per cent stated that they ate less than normal, 30 per cent gave histories of a normal appetite whereas only 27 per cent reported that they ate more than under normal conditions. If the appetite pattern outlined for experimental hyperthyroidism had a counterpart in clinical hyperthyroidism, the poorer appetite levels would be found in the earlier periods of thyrotoxicosis while the normal or increased appetites would be found more often in the later periods. With this in mind, it is interesting to note in Table I the short duration of symptoms associated with poor appetites as compared with the longer duration of symptoms associated with the normal or increased appetites. Since the average age and degree of intoxication were essentially the same for all series, this observation took on added significance. Definite conclusions cannot be drawn from this small volume of material and particularly because all of the findings were not based on controlled objective data. Notwithstanding, I believe that if the appetite changes in clinical hyperthyroidism were carefully studied, the clinical findings would be similar to the experimental findings outlined in this paper. It is obvious that any clinical study contemplated in that direction must exclude the ameliorating influence of iodine, bed rest, roentgen-ray, or other therapeutic agent.

In addition to the changes in appetite, the experiments in this study demonstrated that the liver in hyperthyroidism formed and stored glycogen. This was important not only because of its fundamental significance, but also because it offered an explanation for the confusion in the literature on this question of glycogen storage. As pointed out in the review of literature, the studies of a deranged carbohydrate metabolism in hyperthyroidism took—and for the most part continue to take—their cue from the first communications by Cramer and Krause (7, 26). Cramer and Krause demonstrated that thyroid feeding depleted the hepatic store of glycogen. Their interpretation was that the liver was unable to form and store glycogen. This was a striking demonstration. It introduced a new thought to account for the deranged metabolism of carbohydrate in hyperthyroidism and immediately stimulated investigation of the problem. Unfortunately, the subsequent studies by Cramer and McCall (8, 9, 10, 11), demonstrating that glycogen was formed and stored by the liver, did not appear until after a lapse of 4 years. In the interim the die was cast, for the studies of this derangement adhered to the precedent laid down in the first papers by Cramer and Krause. In following this precedent the experiments were based on short periods of observation. The practice was to administer thyroid for 1 or 2 weeks, occasionally for 3 weeks and rarely for periods of 2 or more months. When this acute experiment is interpreted in terms of the appetite pattern, it is understood why there was reported with such unanimity a depletion in the hepatic store of glycogen. Normally, the hepatic store of glycogen is of labile construction.

Hyperthyroidism increases this lability so that the liver not only binds glycogen loosely but releases it readily. Now, when there was superimposed on this fleeting structure an augmented metabolism and a decreased appetite it is clear why experiments interrupted in the early periods of thyroid feeding revealed a shortage in the hepatic store of glycogen. Had the administration of thyroid been continued until the appetite was established on a higher level and then the experiments interrupted—higher values for the glycogen content of the liver would have been reported. The evidence presented in this study bears out this interpretation.

In concluding this discussion of the changes in appetite and glycogen content of the liver, a plan is outlined that is believed to account for the series of changes observed in experimental hyperthyroidism. With the institution of thyroid feeding the following sequence is noted. After a latent period of 1 to 3 days there is a loss of appetite. The loss of appetite is associated with a corresponding loss in weight and impoverishment in the hepatic store of glycogen. The extent to which the hepatic store of glycogen is impoverished is determined by the degree of intoxication and the level to which the appetite is depressed. If the administration of thyroid is continued, a second period of improvement follows. The appetite improves, but the improvement is variable. In some animals the appetite never recovers from its initial fall and continues at a low ebb for the remainder of the experiment. In other animals the improvement ranges somewhere between the exhausted level and the normal intake. In still others and this is the exception and not the rule—the appetite increases to exceed the normal intake. With the improved appetite there is a gain in weight and replenishment in the hepatic store of glycogen. The maximal point of improvement attained in the second period marks the beginning of the third period. In the third period the appetite is sustained on an improved level. As the third period progresses the disproportion between the food intake and augmented metabolism increases. This is manifested by a progressive loss in weight and lessening in the glycogen store of the liver. After a long interval the third period gradually merges into the fourth and last period of thyroid feeding. The last period, depicting the collapse in animal economy, begins with a decline of the appetite from its sustained level. The decline is at first gradual, then accelerates, and in a short period develops into a complete anorexia. This is associated with a precipitous fall in weight and exhaustion of the hepatic store of glycogen. The animal develops a profound muscular weakness and dies from exhaustion.

SUMMARY

1. An appetite pattern of four periods or phases was associated with the prolonged administration of thyroid.

2. The amount of food taken by an animal during the period of thyroid administration was frequently less than the amount of food taken under normal conditions.

3. In one hundred cases of clinical hyperthyroidism the appetite pattern was similar to the pattern observed in experimental hyperthyroidism.

4. Direct and indirect experimental evidence demonstrated that the liver in hyperthyroidism formed and stored glycogen.

5. The appetite level maintained by an animal during the period of thyroid feeding had a direct influence on the quantity of glycogen stored in the liver.

6. The degree of intoxication, experimentally determined by the amount of thyroid administered, had a direct influence on the quantitative store of hepatic glycogen.

7. The time element, as determined by the duration of thyroid feeding, had only a relative influence on the hepatic store of glycogen.

BIBLIOGRAPHY

1. Burn, J. H., and Marks, H. P. The relation of the thyroid gland to the action of insulin. J. Physiol., 1925, 60: 131.
2. Carlson, A. J., Rooks, J. R., and McKie, J. F. Attempts to produce experimental hyperthyroidism in mammals and birds. Am. J. Physiol., 1912, 30: 129.
3. Charvát, J. Metabolic reflexes. Casop. lék. česk., 1928, 67: 533. Quoted by John, H. J. loc. cit. (24).
4. Charvát, J., and Gjurič. The question of liver and tissue glyco-regulation. Rozpr. II třídy české Akad. 1926, No. 26, p. 36. Quoted by John, H. J. loc. cit. (24).

5. Cori, C. F. Mammalian carbohydrate metabolism. Physiol. Rev., 1931, 11: 143.
6. Cramer, W. On the thyroid-adrenal apparatus and its function in the heat regulation of the body (preliminary communication). Proc. Physiol. Soc., 1916, 50: 38.
7. Cramer, W., and Krause, R. A. Carbohydrate metabolism in its relation to the thyroid gland. The effect of thyroid feeding on the glycogen content of the liver and on the nitrogen distribution in urine. Proc. Roy. Soc. Lond. Ser. B, 1912–1913, 86: 550.
8. Cramer, W., and McCall, R. On the carbohydrate metabolism in experimental hyperthyroidism. Proc. Physiol. Soc., 1916, p. 36.
9. Idem. Carbohydrate metabolism in relation to the thyroid gland. II. The effect of thyroid feeding on the gaseous metabolism. Quart. J. Exper. Physiol., 1917, 11: 59.
10. Idem. Carbohydrate metabolism in relation to the thyroid gland. III. The effect of thyroidectomy in rats on the gaseous metabolism. Quart. J. Exper. Physiol., 1918–1920, 12: 81.
11. Idem. Carbohydrate metabolism in relation to the thyroid gland. IV. The effect of thyroid feeding on the gaseous metabolism of thyroidectomized rats. Quart. J. Exper. Physiol., 1918–1920, 12: 97.
12. Denis, W., Aub, J. C., and Minot, A. S. Blood sugar in hyperthyroidism. Arch. Int. Med., 1917, 20: 964.
13. DuBois, E. F. Clinical calorimetry. IVX. Metabolism in exophthalmic goiter. Arch. Int. Med., 1916, 17: 915.
14. Eppinger, H., Falta, W., and Rudinger, C. Ueber die Wechselwirkungen der Druesen mit innerer Sekretion. Ztschr. f. klin. Med., 1908, 66: 1.
15. Folin, O., and Wu. The determination of sugar in blood and normal urine. J. Biol. Chem., 1926, 67: 357.
16. Frazier, W. D., and Ravdin, I. S. The use of vitamin B_1 in the pre-operative preparation of the hyperthyroid patient. Surgery, 1938, 4: 680.
17. French, H. E. The comparative toxicity of different animal tissues to animals susceptible to thyroid feeding. Am. J. Physiol., 1912, 30: 56.
18. Gardner-Hill, B. H., and Brett, P. C., and Smith, J. F. Carbohydrate metabolism in myxedema. Quart. J. Med., 1925, 18: 327.
19. Garrod, A. E. Lettsomian lectures on glycosuria, III. Lancet, 1912, 1: 629.
20. Geylin, H. R. The carbohydrate metabolism in hyperthyroidism as determined by examination of blood and urine. Arch. Int. Med., 1915, 16: 975.
21. Hamman, L., and Hirschman, I. Studies on blood sugar. Arch. Int. Med., 1917, 20: 761.
22. John, H. J. Carbohydrate metabolism in hyperthyroidism. Endocrinology, 1927, 11: 497.
23. Idem. A study of 1,100 glucose tolerance tests. Med. J. & Rec., 1930, 131: 287.
24. Idem. Hyperthyroidism showing carbohydrate metabolic disturbances. J. Am. M. Ass., 1932, 99: 620.
25. Johnston, J. A. Carbohydrate metabolism. II. Rôle of the thyroid gland. Am. J. Dis. Child., 1934, 48: 1015.
26. Krause, R. A., and Cramer, W. On the effect of thyroid feeding on nitrogen and carbohydrate metabolism. Proc. Physiol. Soc., 1912, May 18, p. 23.
27. Kuriyama, S. The influence of thyroid feeding upon carbohydrate metabolism. Am. J. Physiol., 1917, 43: 481.
28. Magnus-Levy. Von Noordens' Metabolism and Practical Medicine, 1907, vol. 3, p. 983.
29. Marks, H. P. Effect of thyroid feeding on sugar tolerance. J. Physiol., 1925, 60: 402.
30. McElroy, J. S., Schuman, E. B., and Ritchey, J. O. A study of the changes in serum cholesterol, gastric secretion and carbohydrate metabolism in patients with toxic goiter. Ann. Int. Med., 1938, 12: 106.
31. Mirsky, A., and Broh-Kahn, R. H. The effect of experimental hyperthyroidism on carbohydrate metabolism. Am. J. Physiol., 1936, 117: 6.
32. Richardson, H. B., Levine, S. Z., and DuBois, E. F. The storage of glycogen in exophthalmic goiter, XLI. J. Biol. Chem., 1926, 67: 737.
33. Sahyun, M. Determination of glycogen in tissues. J. Biol. Chem., 1931, 93: 227.
34. Sanger, B. J., and Hun, E. G. The glucose mobilization rate in hyperthyroidism. Arch. Int. Med., 1922, 30: 397.
35. Wilder, R. M. Hyperthyroidism, myxedema and diabetes. Arch. Int. Med., 1926, 38: 736.
36. Wilder, R. M., and Sansum, W. D. Glucose tolerance in health and disease. Arch. Int. Med., 1917, 19: 311.

OBSERVATIONS ON THE ROENTGENOLOGICAL EVIDENCE OF FETAL DEATH

HERBERT THOMS, M.D., F.A.C.S., New Haven, Connecticut

ATTENTION was first called to the value of roentgenography as a means of determining fetal death *in utero* by D. A. Horner in 1921 in a thesis presented before the Chicago Gynecological Society. At that time he stated that "overriding of the skull bones with cephalic asymmetry are signs of fetal death." Since that time a good deal of attention has been given to this subject by various observers and in 1931 Szello presented a summary of the changes in the fetal skeleton which might give diagnostic information. These are: (1) flattening of the fetal skull; (2) marked bending of the spinal column, which is the earliest sign; (3) overlapping of the skull bones with decrease in the radius of the skull; (4) later, separation of the skull bones; (5) asymmetry of the skull; (6) failure of the size of the bones to correspond with the duration of pregnancy; (7) haziness of the bony landmarks and contours, or entire disappearance of the bony shadows.

It seems to be well established from autopsy findings of the newborn that brain tissue is the first to show degenerative changes, and it is Horner's contention that skull collapse as a result of brain collapse is the first of the skeletal changes to be noted after fetal death. This sequence seems to be well authenticated by numerous observers, but whether skull collapse to the point of overlapping of the skull bones takes place in all instances within a relatively short time after brain collapse is open to question. With newer and better roentgen technique it may be possible to demonstrate brain collapse in the absence of, or before, such overlapping takes place. There is, however, some question as to whether overlapping in itself is pathognomonic of fetal death. DeLee states that he has noted such overlapping in a living fetus, and we have noticed the same thing, as evidenced in the accompanying roentgenogram (Fig. 1) taken during studies on fetal cephalometry 3 days before labor occurred with delivery of a living child. The question, therefore, remains controversial, for in 1936 Horner stated "The fact nevertheless remains that overlapping of the skull bones is still the last word in the establishment of roentgen diagnosis of ante partum fetal death." We recently observed a case of fetal death *in utero* in our wards which seemed to show roentgen evidence of brain collapse in which no overlapping was demonstrable at any time.

The essential history may be thus summarized. A trigravida primipara was physically and subjectively well throughout her pregnancy, which was expected to terminate October 10, 1939. On October 19, 1939, she was seen in the prenatal clinic at which time she stated that she had not felt movement for the

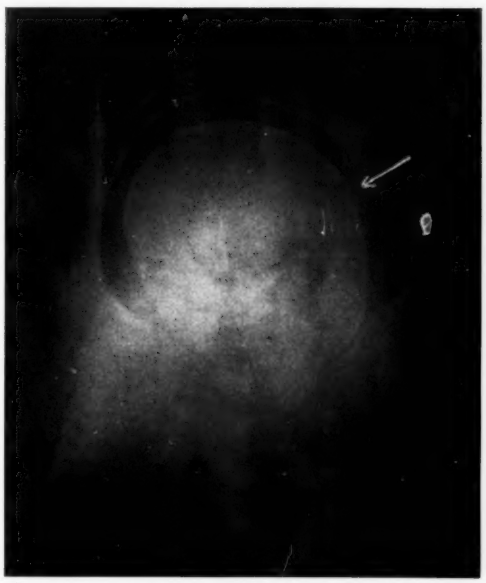
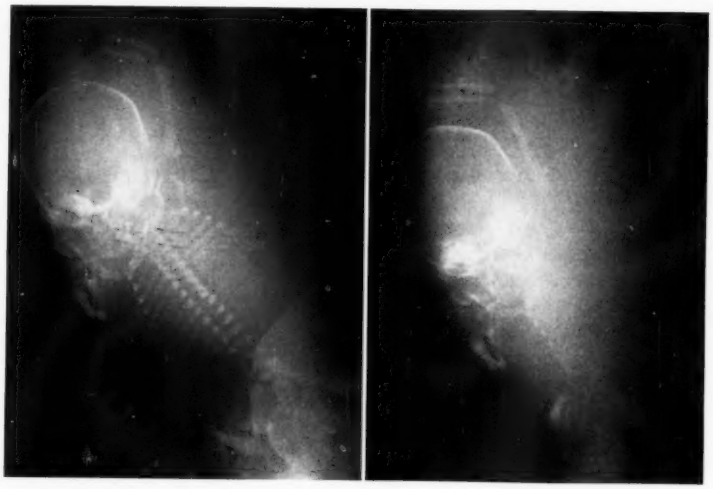


Fig. 1. Roentgenogram made 3 days before labor showing overlapping of skull in living fetus.

From the Department of Obstetrics and Gynecology, Yale University School of Medicine.

Fig. 2. Roentgenogram showing no evidence of overlapping or evidence of fetal death.

Fig. 3. Roentgenogram 24 hours after Figure 2 was taken. Some changes noted in skull.



Figs. 4 and 5. Case 2. The patient, a 35 year old tripara, entered hospital December 20, 1939, for suspected fetal death *in utero* at 6 months' gestation. No movements felt by patient for several days and breasts said to be diminishing in size. Fetal heart and other usual sounds not heard. Roentgenogram shown in Figure 4, at left, taken December 21, 1939, that in Figure 5 taken December 22, 1939. Absolutely no change in position of fetal parts noted. One film may be exactly superimposed over the other. No significant skull changes noted. Stillborn macerated fetus expelled after medical induction.

past 5 or 6 days. No fetal heart or movements could be demonstrated, and a peculiar silence was noted over the entire uterus. Fetal death was suspected and the patient entered the hospital for further observation. A flat film (Fig. 2) of the abdomen taken at this time showed no evidence of overlapping or other changes which could be regarded as evidence of fetal death. Twenty-four hours later another similar film was taken which showed changes in the skull (Fig. 3) as evidenced by depression or cupping of the anterior fontanel and a distinct change in the frontal suture line leading to the fontanel. In addition, the bones of the lower extremities and other portions of the fetal skeleton showed so little change in position that this film could be almost exactly superimposed over that taken 24 hours previously. Seventy-two hours after admission vaginal examination was done by the author in order to determine whether or not skull changes could be noted by this maneuver, but, although the cervix was 3 centimeters dilated, no evidence of overlapping or skull collapse could be noted. At this time the membranes were ruptured artificially and 24 hours later the patient spontaneously expelled a stillborn fetus which showed signs of maceration.

In further discussion of this subject it seems evident that at the present time there is no definite roentgenological procedure which in all cases can be considered pathognomonic of fetal death *in utero* within a first week after this event has taken place. Recognizing the fact that brain collapse is an early change, our attention should be drawn to the consideration of this change in viewing roentgenograms. It may be that serial roentgenograms taken at 24 hour intervals, with particular study of the fontanels and sutures, may give suggestive information concerning brain collapse, as in the case here cited. In addition, *serial roentgenograms may give evidences of a lack of spontaneous fetal movement as likewise noted.*

Finally, the well known clinical signs of fetal death should be thoughtfully interpreted in all cases, for here as in other fields of medical investigation roentgenological evidence serves as an adjunct which is both useful and important to diagnostic skill.

REFERENCES

1. DeLee, J. B. The Principles and Practice of Obstetrics, 7th ed., p. 306. Philadelphia and London: W. B. Saunders Co., 1938.
2. Horner, D. A. Am. J. Obst. Gynec., 1936, 32: 67.
3. Szello, F. Arch. f. Gynaek., 1931, 145: 495.

THE INFLUENCE OF HOT AND COLD APPLICATION UPON GASTRIC AND INTESTINAL MOTOR ACTIVITY

J. DEWEY BISGARD, M.D., and DAN NYE, M.D.,
Omaha, Nebraska

FROM time immemorial hot and cold applications have been utilized in the treatment of certain lesions and functional disturbances of the gastro-intestinal tract. These applications are made directly through the fluids ingested and through those used for irrigation of the stomach and bowel and indirectly by the external application of hot and cold packs. As generally employed, ice is given by mouth and applied externally in cases in which a sedative or inhibitory effect upon gastro-intestinal motor and secretory activity is indicated; and hot drinks, irrigations, and compresses are administered when stimulation is desired. To examine the validity of this concept the physiological investigation herein reported was carried out.

These studies represent a continuation of some previously reported (2). As in the previous studies continuous kymographic recordings were made of gastro-intestinal motor activity. These recordings registered the variations in pressure within the stomach and bowel resulting from tonus and peristaltic contractions of these organs during a period of observation.

Rubber balloons (on Miller-Abbott tubes) were introduced into the stomach through the esophagus, into the small bowel via the esophagus and ileostomy stomas and into the large bowel through colostomy openings. Variations of pressure upon these inflated balloons were transmitted to ink-writers through U-tube manometers containing bromoform. The apparatus with a balloon in the ileum passed through an ileostomy stoma is shown in Figure 1. All records of the stomach and small bowel were made upon essentially normal individuals, those of the colon upon patients who had had resections of rectal carcinomas from 1 year to several weeks previously.

From the Department of Surgery, College of Medicine, University of Nebraska.

All studies were made while the gastro-intestinal tract was in a state of fast. The experimental procedure in each instance consisted of a preliminary recording of normal peristaltic activity over a period of 30 minutes or more. As soon as a consistent normal record had been obtained, each of the following influences were brought to bear at successive periods of observation: (1) the abdominal wall was completely covered with hot water bottles for 30 minutes, (2) the abdominal wall was covered with ice bags for 30 minutes, (3) both thighs were covered with hot water bottles for 30 minutes, (4) both thighs were covered with ice bags for 30 minutes, (5) hot water was administered orally, (6) iced water was administered orally. The effect of these various influences will be discussed under their respective headings. Periodically during the period of recording of gastric motility samples of gastric contents were aspirated and analyzed for acidity. These findings are recorded in Table I. Three samples were taken from each patient. The first one was taken immediately before the application of the pack and the other two 10 and 60 minutes following the application.

Complete series of records of responses of the stomach were obtained in 8 patients, of the small bowel in 6, and of the colon in 4. Since the individual responses in each group were consistent in respect to pattern and varied only in degree they will be discussed collectively in terms of the response typical of the organ and the experimental factor.

1. Hot packs applied to the abdominal wall had an inhibitory influence upon gastric motor activity. For a period of 5 to 10 minutes following the applications there was no change. Then followed a reduction of tone and of both frequency and amplitude of peristalsis. This inhibitory influence lasted from 20 to 45 minutes. Samples of gastric

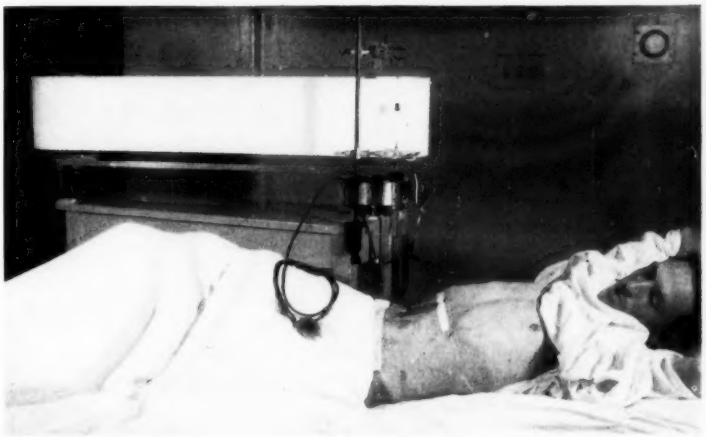


Fig. 1. Patient with an ileostomy. The tube emerging from the stoma connects an inflated balloon within the ileum to the U tube manometer. An identical tube and balloon are displayed on the sheet across the patient's thighs. Pressure changes within the bowel are transmitted from the balloon to the ink-writer through the U tube. The ink-writer records the pressure changes upon the kymographic drum.

juice were obtained for analysis from 6 of the 8 patients. These analyses showed no appreciable change in the acidity. For the individual figures see Table I.

Both small and large bowel showed the same inhibitory response; also a slight lessening of tone. The response appeared after an interval varying from 5 to 10 minutes during which time peristalsis continued unchanged or showed slight stimulation. The inhibition lasted from 15 to 40 minutes. Illustrative records are shown in Figure 2.

2. Ice packs, applied by covering the abdominal wall with ice bags, caused vigorous motor responses in all 3 segments of the gastro-intestinal tract. This response in each instance was preceded by a period of normal activity lasting from 4 to 18 minutes. The subsequent periods of increased activity varied from 20 to 50 minutes and the stomach showed the longest and most vigorous response. Representative tracings appear in Figure 3.

Samples of gastric contents were obtained from 5 patients. In 1 patient who had an achlorhydria there was no change but in the 4 others there was a rapid and big increase in both free and total acids. The figures for the individual analyses are recorded in Table I.

3. The difference in the response to hot and cold applications was shown strikingly by the alternate application of these thermal agents.

In this group of experiments hot packs were applied to the abdominal wall for 30 minutes and records obtained during this period and

TABLE I.—GASTRIC ACIDITY

	Hot packs to abdomen			Cold packs to abdomen		
Cases	Before	After	Net change	Before	After	Net change
1	10–30	14–35	4–5	14–35	38–60	24–25
2	30–45	35–50	5–5	14–34	39–58	25–24
3	0–10	0–10	0–0	0–8	0–10	0–2
4	18–32	24–36	6–4	14–30	38–88	24–58
5	28–48	25–48	3–0	30–52	48–95	18–43
6	22–32	22–30	0–2			

	Hot packs to thighs			Cold packs to thighs		
Cases	Before	After	Net change	Before	After	Net change
1	14–36	10–36	4–0	17–40	36–59	19–19
2	32–50	37–56	5–6	28–45	42–80	14–35
3	0–5	0–6	0–1	0–6	0–6	0–0
4	10–32	18–41	8–9	14–38	36–86	22–48
5				24–40	42–92	18–52

Case 3, patient with achlorhydria; also showed no response to histamine.

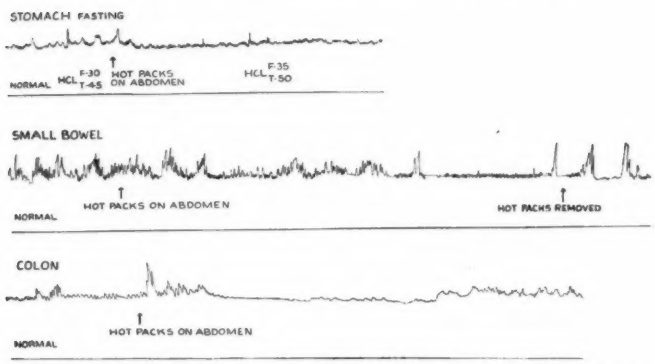


Fig. 2. Recordings of motor activity of the stomach, small bowel, and colon before and after covering the abdominal wall with hot water bottles. After an interval of 5 to 10 minutes, tonus became slightly diminished and peristalsis greatly inhibited in all three segments. Note that the acidity of the gastric contents remained unchanged.

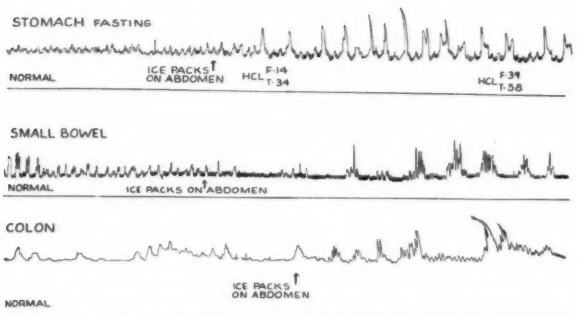


Fig. 3. The application of ice bags to the abdominal wall produced vigorous motor responses in stomach, small bowel, and colon, as indicated by an increase in tonus and in the amplitude and duration of contractions. Note that these responses did not come on immediately but followed a latent interval varying from 5 to 15 minutes. Also note the big increase in gastric acidity.

for 10 minutes following removal of the packs. Ice bags were then applied and the recording continued for another hour. Records of this type were obtained in 5 patients, the stomach in 3, and the colon in 2. In each instance inhibition followed the application of hot packs after a latent interval of 5 to 10 minutes. Almost immediately following the application of ice packs both stomach and colon, still inhibited from the hot packs, showed fairly vigorous motor responses. These motor effects lasted as long as 60 minutes.

Gastric analyses were made in 2 cases and both showed no change in free and total acids during the period of hot applications but very marked increases following the application of ice. See Table I and Figure 4.

4. The influence of repeated applications of hot and cold packs to the abdomen was studied and it was found that the original responses were repeated. As reported, both inhibitory and motor influences terminate after intervals of 20 to 60 minutes. Clinically, these therapeutic thermal agents are continued over periods of several hours or days, either at constant temperatures or more often at the varying temperatures resulting from re-applications. For this reason the influence of the sec-

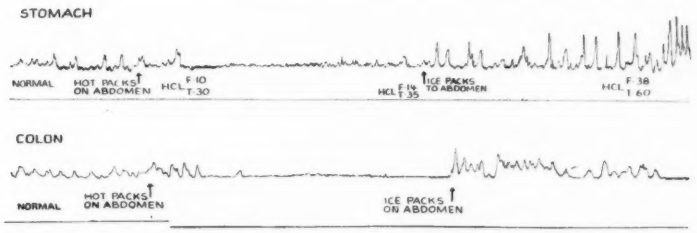


Fig. 4. Recordings of the effects upon the stomach and colon following external hot applications with ice packs. Ice was applied immediately following removal of the hot packs. Note that the inhibitory response to the hot applications was converted almost immediately to the motor response to cold. Note also that gastric acidity remained unchanged during the application of heat and increased greatly following the application of ice.

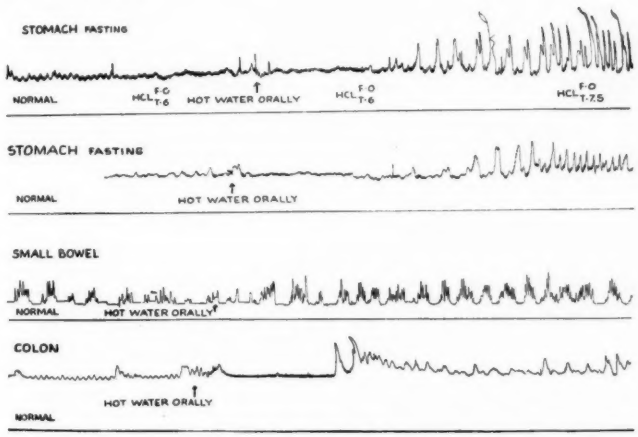


Fig. 5. Hot water taken by mouth caused a vigorous motor response in the stomach and definite but less vigorous stimulation of the small bowel and colon. The periods of increased activity were preceded by intervals of inhibition lasting from 5 to 20 minutes.

ond applications of hot and of cold packs an hour after the effects of the first applications had been dissipated was determined. Recordings were made of the stomach, small bowel, and colon during re-application of hot packs in 2 patients and of ice packs in 1 patient. As in the cases of the first applications heat inhibited and cold increased motor activity. These second responses, however, were lesser in degree and shorter in duration.

5. Hot water (6 ounces) administered by mouth had a pronounced motor effect with increase of both tonus and peristalsis along the entire gastro-intestinal tract. The motor effect became apparent after a period varying from 5 to 15 minutes during which period peristalsis either continued unchanged or was slightly inhibited (Fig. 5).

Gastric analyses in the 3 patients from whom samples were obtained showed a moderate reduction of both free and total acids, presumably the result of dilution. There was, however, less reduction of the acids than in the patients given iced water.

6. Iced water (6 ounces) given by mouth had a slight but definite inhibitory effect upon the stomach and small bowel lasting from 10 to 30 minutes. After this period of inhibition peristalsis became normal or slightly exaggerated. The colon showed no definite response. Gastric acidity was reduced in the 4 patients from whom samples were obtained.

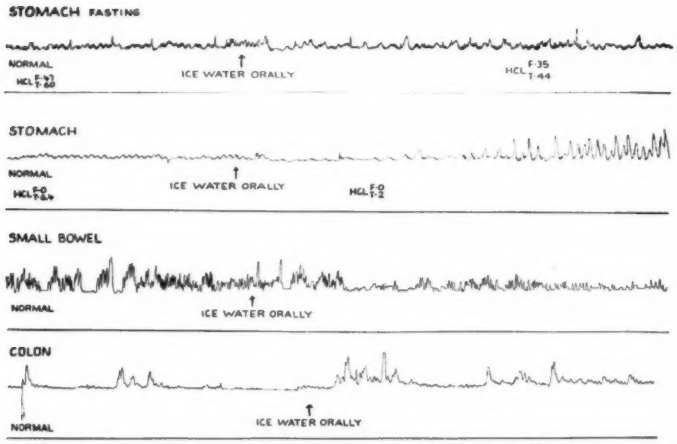


Fig. 6. The administration of ice water by mouth had little or no effect upon gastro-intestinal activity. Note that gastric acidity was decreased; the result, presumably, of both dilution and inhibition.

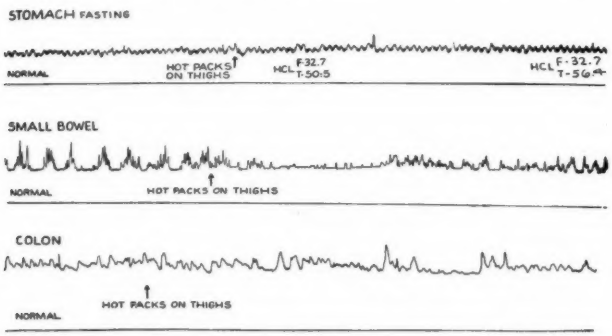


Fig. 7. The application of hot water bottles to both thighs had no appreciable effect upon gastro-intestinal activity, and none upon gastric acidity. The small bowel shows some inhibition.

Presumably this was more than would result from simple dilution from water drunk. Sample records are shown in Figure 6.

7. The application of hot water bottles to the thighs had no effect upon the colon. There was a slight inhibitory influence lasting from 3 to 10 minutes upon the stomach and small bowel (Fig. 7).

Gastric analysis in 4 cases showed no appreciable increase in free or total acids.

8. Ice bags applied to the thighs had no effect upon the colon and had either no, or only a slight, motor effect upon the small bowel. The stomach in all but 2 instances manifested a moderate to vigorous motor response.

In 5 cases the motor response was preceded by an immediate inhibitory one lasting from 3 to 5 minutes. These motor effects lasted from 25 to 45 minutes. Typical records appear in Figure 8.

Studies of the gastric contents were made in 5 patients and in all but 1 there was a sharp rise in both free and total acids (see Table I). The patients who developed no increase in acidity had an achlorhydria and, interestingly, also, there was no appreciable motor response. The recording from this patient is shown in Figure 9.

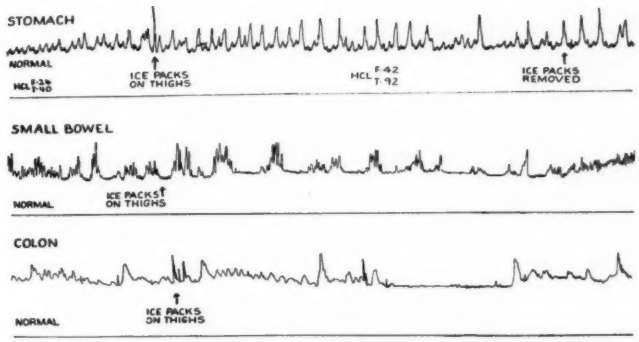


Fig. 8. Ice packs applied to both thighs increased both gastric acidity and motor activity of the stomach. The ileum and colon showed no definite or consistent response.

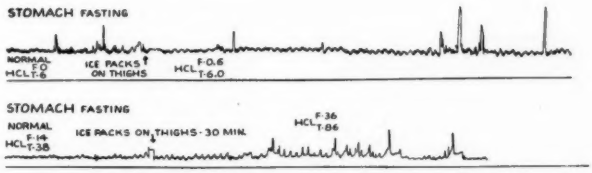


Fig. 9. The contrast of the reaction of the stomach to the application of ice to the thighs in these two patients suggests a close association between gastric acidity and motor activity. The stomach with achlorhydria showed no response. Both acidity and motor activity remained unchanged. In the stomach with normal acidity, however, the application of ice was followed by a big increase in both acidity and peristalsis.

ANALYSIS OF STUDY

Normally the motor activity of the gastrointestinal tract varies tremendously from minute to minute and hour to hour. It is acutely sensitive to widely varied influences and is stimulated or inhibited by such factors as the emotions, the reactions to associations with the senses of sight, taste, and smell, the physical states of sleep and fatigue, and the direct factors of hunger and ingestion of water and food. Since some of these influences, notably the emotions, cannot be controlled, studies of motor activity are subject to gross errors of interpretation. Since, however, the responses which followed the applications of hot and cold were consistently characteristic in pattern in repeated observations they have been interpreted the results of experimental factors. These responses may be summarized as follows: Heat applied to the abdominal wall inhibited motor activity of the stomach, small bowel, and colon. Conversely, cold stimulated activity. When applied directly to the wall of the stomach by the temperature of the water drunk the response to these thermal agents was reversed. Heat stimulated and cold had little or no effect upon both gastric and intestinal motor activity.

Applied to the thighs heat had no effect and cold influenced only the stomach, where it produced a moderate motor response. Hot applications did not alter the acidity of the gastric contents, while cold ones caused big increases in both free and total acids. Since the application of cold to the thighs as well as to the abdomen produced an increase of both gastric acidity and motor activity it is probable that the increase in acidity was responsible for the motor response. It has been demonstrated by Horton and Brown and others that the chilling of body surfaces causes the liberation of histamine, or a histamine-

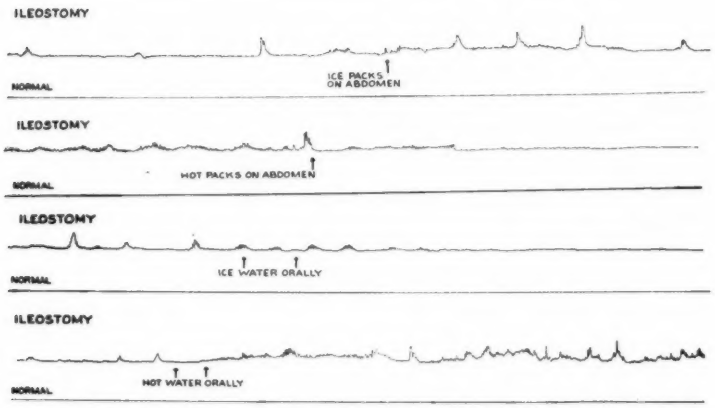


Fig. 10. Recordings of the motor activity of the ileum of the patient shown in Figure 1. Ice applied externally stimulated and taken internally inhibited peristalsis and tone. Hot applications had the reverse effects.

like substance. The stimulating effect of histamine upon gastric secretions is well established and utilized clinically. Thus it may be possible that the increase in gastric acidity following the application of ice resulted from histamine liberated by this application.

In using the terms motor and inhibitory to describe the reactions to hot and cold we appreciate the fallacy in making such a simple interpretation of the pressure changes exerted upon the balloons. These pressure changes are determined not only by the contractions of these organs but also by the patency of the sphincters. For this reason we are now investigating the effect of hot and cold applications upon sphincter tonus. Observations of this type have been made by Todd. In his studies of gastric motility by fluoroscopic observation he found that both hot and cold drinks of milk increased the frequency and vigor of peristaltic waves. Stimulation, however, was greater and much more prolonged with hot than with cold milk, 20 minutes with hot and only 5 to 10 minutes with cold. Also with hot milk the opening of the pylorus was more frequent and more prolonged.

Carlson, using balloons to study hunger contraction in both man and dogs, found that iced water taken by mouth diminished gastric tonus and inhibited hunger contractions but that cold applied externally stimulated contractions. This stimulation, however, was preceded by a brief period during which there was either no effect or an inhibitory one. Wertz and Sterkel and Carlson found that exposure of the naked human body to temperatures of 4 to 10 degrees Centigrade provoked a motor response in the stomach. Jaworski observed in man and Schule and Mueller in dogs, a reduction of tonus and peristalsis following the ingestion of iced water. Atkinson reported that ice placed directly upon the abdominal wall of dogs caused a decrease in gastric tonus and peristalsis.

With the exception of this latter reference, all observations reported above are consistent and are in agreement with our findings. That this discrepancy is probably more apparent than real has been demonstrated by the studies of Sato. Using rabbits he recorded the intragastric pressure changes exerted upon indwelling balloons as a result of external applications of ice. He found that the gastric response was dependent upon the depth in the tissues to which the lowering of temperature was carried by conduction. If the cooling effect of ice did not extend deeper than the abdominal wall the stomach showed a motor response but if it extended to the wall of the stomach itself its motor activity became inhibited. Thus the same inhibitory action is produced by the actual cooling of the stomach whether indirectly by conduction through the abdominal wall or directly by contact with cold fluids

administered by mouth. However, it seems extremely unlikely that the cooling effect of ice bags as used clinically ever extends deep enough to involve the wall of the stomach.

In an attempt to determine the modus operandi of cold applications Sato repeated his studies upon three groups of rabbits; in the first, both vagi were sectioned; in the second, the celiac and superior mesenteric ganglia were excised; and in the third group, the spinal cord was divided at the level of the second thoracic vertebra. Cooling of the abdominal wall in the first group had a very slight inhibitory effect, in the second group a pronounced motor effect, and in the third no effect. In all 3 groups, however, cooling of the wall of the stomach caused a decrease in tone and peristalsis. From this evidence he concluded that the motor responses to the application of ice result from the action of somatic stimuli upon the parasympathetic and sympathetic innervations of the stomach whereas the inhibitory responses result directly from the cooling of the tissues of the wall of the stomach.

The results of our investigation, we believe, provide some physiological data which can be used as a basis for guidance in the proper uses of hot and cold application. Some of the evidence is conclusive and its clinical application definite. For example, if it is beneficial as is generally believed that the gastro-intestinal tract be inhibited and placed at rest in so far as possible in the presence of inflammatory lesions such as appendicitis and peritonitis and of bleeding lesions such as bleeding peptic ulcers, then hot application and not ice bags are indicated. In these conditions the motor effect of the cold applications which are so commonly employed may be definitely deleterious. In the case of peptic ulcers the increase in gastric acidity following the application of cold is also undesirable and a possible contra-indication. In respect to the treatment of bleeding peptic ulcers the temperature of fluids administered by mouth deserves consideration. Disregarding the controversy between those who advocate complete starvation and those who feed patients with actively bleeding ulcers, attention is directed to the evidence that iced fluids cause greater reduction of gastric acidity than hot ones and have little or no effect upon peristalsis. In addition cold produces vasoconstriction, theoretically a possible virtue in these cases. Certain clinicians lavage bleeding stomachs and for the same reasons enumerated, it would appear that the solutions used should be cold and possibly iced.

From the physiological data which has been presented it appears that ice packs would be more effective than hot application for purposes of expelling gas and relieving distention and that cold water by mouth would cause less gastric disturbance than warm water in recent postoperative cases. The physiological problem in this group, however, differs from that in the preceding one in one important aspect, namely motility. The movement of gastric and intestinal contents involves factors in addition to those studied in this investigation. It involves the proper integration of motor activity in the adjacent segments of the stomach and bowel and of their sphincters. It is well established that peristalsis regardless of vigor is ineffectual when disorganized. In the normal process of both segmental and mass movements of intestinal contents, the various segments of bowel contract and relax alternately in well integrated fashion. As a given segment contracts and expels its contents the adjoining distal segment relaxes to receive it. Failure of this distal segment to relax not only interferes with the normal movement of intestinal contents but also gives rise to cramp-like pain (gas pain). Thus under these circumstances the increased peristaltic activity resulting from cold applications might serve only to aggravate the disturbance and increase the patient's discomfort. Conversely, hot compresses by virtue of their inhibitory effect may be more conducive to co-ordinated action. Clinically, hot applications are definitely more effective than cold ones for the relief of colicky pain. But it is our impression, based upon recent comparative clinical observations, that cold applications are more effective in relieving distention.

In regard to the first fluids taken by mouth by postoperative patients we have observed no difference in the response to temperatures of cool and warm except that cool fluids are more palatable. However, iced water has been definitely less well tolerated.

CONCLUSIONS

1. Gastro-intestinal motor activity is inhibited by the application of heat to the abdominal wall and by iced water taken by mouth. It is stimulated by the application of ice to the abdominal wall and by the ingestion of hot water by mouth.

2. External cold applications increase gastric acidity, increasing both free and total acids. In a subsequent publication it will be proposed that this response be utilized in the test for true achlorhydria. By simply immersing the hands in iced water for a few minutes a response similar to that resulting from the subcutaneous injection of histamine can be obtained.

3. The ingestion of iced water diminishes the secretion of acids by the stomach.

BIBLIOGRAPHY

1. Atkinson, H. V. The effect of external and internal application of heat and cold on the muscular activity of the stomach of unanesthetized dogs. J. Pharmacol. & Exper. Therap., 1928, 33: 321.
2. Bisgard, J. D., and Johnson, E. K. The influence of certain drugs and anesthetics upon gastro-intestinal tone and motility. Ann. Surg., 1939, 110: 802.
3. Carlson, D. J. The Control of Hunger in Health and Disease. Chicago: The University of Chicago Press, 1916.
4. Horton, B. T., and Brown, G. E. Histamine-like effects on gastric acidity due to cold. Proc. Staff Meet. Mayo Clin., 1932, 7: 367.
5. Jaworski, W. Vergleichend experimentelle Untersuchungen ueber das Verhalten des Kessinger und Karlsbader Wassers. Arch. f. klin. Med., 1884, 35: 38.
6. Mueller, J. Ueber den Einfluss der Temperatur der Speisen auf die Magenfunktionen. Ztschr. f. Diaetet. u. physik. Therap., 1905, 8: 587–594.
7. Sato, S. Ueber den Einfluss der Bauchwandabkubling auf den Magenzustand. Tohoku J. Exper. Med., 1935, 27: 87.
8. Schule, D. A. Untersuchungen ueber die Secretion und Motilitat des normalen Magens. Ztschr. f. klin. Med., 1896, 29: 49.
9. Todd, T. W. Behavior Patterns of the Alimentary Tract. Baltimore: Williams & Wilkins Company, 1930.
10. Wertz, W., and Sterkel, D. Ueber den Einfluss der Kalte auf die Gestalt des Magens. Med. Klin., 1920, 15: 980.

CANCER AND ITS RELATIONS TO PREGNANCY AND DELIVERY, TO MARITAL AND SOCIAL STATUS

II. Cancer of Organs Other Than Reproductive; Total Cancer Mortality

SIGISMUND PELLER, M.D., Baltimore, Maryland

DIVIDING the male population of England and Wales into 5 social classes, Stevenson (1928) found an inverse change between the social position and the mortality rates from cancer of the skin, nose, pharynx, larynx, esophagus, and stomach, whereas the mortality from cancer of all other parts of the body remained unaffected. These parts were therefore supposed to be "inaccessible" to external irritants. That conclusion was broadly confirmed in 1938 by the analysis given for the years 1930–1932 by Stocks. The same results proved valid also for women. The difference in rates between accessible and inaccessible organs is the more surprising since it is a well known fact that the "inaccessible" lungs, urinary bladder, liver, and bones, are very likely to be affected by certain occupational risks.

By analyzing the cancerous reactions of the uterus, ovaries, and breast on the basis of social and biological conditions we learned of responses which counterbalanced one another. Therefore, the cancer totals for all the reproductive organs taken together showed very little of these organ-specific reactions. The situation regarding inaccessible organs is entirely different; none of them clearly is influenced by the differences in social level. However, one must distinguish between the kind of social grading applied here (e.g., social class) and the social grading in general.

The marital status and cancer of the accessible and inaccessible organs. The marital status implies a social grading in itself. This grading reveals differences in cancer mortality. Widows show a higher incidence of cancer of the stomach than do married women, and married women have higher rates than spinsters. Other accessible organs such as the skin and lip, mouth, pharynx, and esophagus, do not show any definite or outstanding trend. The so called inaccessible organs however display differences according to the marital status. In the age groups above 54 these differences are not smaller than those shown for the total of accessible or for the total of the reproductive organs. Widows again have the highest and spinsters the lowest rates, the differences being highly significant (Table I). The differences in rates between single persons and widows are greater than those between the first and fifth class. Therefore, factors other than social status must account for these differences.

Some of the differences are due to the relationship between reproductive activity and cancer of the gall bladder. Of the women suffering with gall-bladder disease there are fewer oligoparæ and a greater number of multiparæ than will be found in the women with cancer of the cervix (Peller and Stoehr). As to cancer of the biliary system, the rates for widows do not differ from those for married women but those for both are significantly higher than for single women (age groups above 55). (Table II.)

In compiling statistics regarding the inaccessible organs it is cancer of the biliary system that brings the rates higher for married women over 54 years of age than for spinsters, and it is cancer of the colon and pancreas that reduces the rates for married women over widows. The differences in the rates for cancer of the colon are significant; the rates for the rectum, for the urinary and respiratory organs, for the thyroid, the brain, and the bones show no differences as regards widows and married or single women (Tables III and IV).

Fellow in Biology in the School of Hygiene and Public Health, Johns Hopkins University.

TABLE I.—ENGLAND AND WALES, 1930–1932. CANCER MORTALITY OF WOMEN BY AGE, MARITAL STATUS AND "ACCESSIBILITY" OF THE ORGANS

Age	25—	35—	45—	55—	65—	70—
1. Number of women living in 1931						
Spinsters	1105	573	431	306	109.7	151.2
Married	2203	2222	1897	1213	319.1	257.1
Widows and divorced	41.4	159.1	305.2	440.2	263.9	589.1
2. Cancer of accessible organs						
a. Number of deaths						
Spinsters	77	154	459	720	473	1040
Married	168	713	1874	2996	1513	1943
Widows and divorced	2	65	367	1366	1374	5332
b. Death rates from cancer of all accessible organs (per 100,000)*						
Spinsters	2.3	8.9±0.8	35.5±1.6	78±2.9	144±6.6	229±7.1
Married	2.5	10.7±0.4	33 ±0.7	82±1.1	158±4.0	252±5.7
Widows and divorced	1.6	13.6±1.6	40 ±2.1	103±2.7	174±4.7	302±4.1
c. Death rates from cancer of the stomach						
Spinsters	1.6	6.8	25	56±2.6	106±5.6	166±6.0
Married	2.0	8.1	24	63±1.3	130±3.7	199±5.0
Widows and divorced	1.6	9.0	31	81±2.5	142±4.2	222±3.5
3. Cancer of inaccessible organs†						
a. Number of deaths						
Spinsters	180	368	857	1376	874	1936
Married	397	1237	3297	5577	2637	3527
Widows and divorced	7	80	623	2234	2357	8738
b. Death rates from cancer of the inaccessible organs						
Spinsters	5.4	21±1.0	66±2.4	150±4.0	266±8.9	427±9.7
Married	5.8	18.5±0.5	57±1.0	153±2.0	275±5.3	457±7.7
Widows and divorced	5.6	17±1.9	68±2.7	169±3.5	298±6.1	494±5.2

*Skin, lip, all parts of the mouth including jaw, pharynx, esophagus, and stomach.
†All other digestive organs, the respiratory organs, kidney and bladder, the thyroid, the brain, the bones excluding the jaw, and undefined organs.

MORTALITY ACCORDING TO MARITAL STATUS

In our calculations in the age groups above 54 years, spinsters have higher rates for cancer of the reproductive organs than do married women and lower rates for cancer of accessible and inaccessible organs. Thus, in spite of the considerable differences in rates between single and married women as regards the various organs—the cervix and body of the uterus, the ovaries, breast, and gall bladder—the figures representing the total cancer mortality reflect very little of these differences.

Comparing the death rates from cancer for single women and widows the latter in all age groups is significantly higher. In younger women the differences are almost entirely due to the lower frequency of cancer of the reproductive organs; in older women the differences in rates are considerable for cancer of the accessible as well as of the inaccessible organs.

With the exception of the age group 25 to 34 years the cancer mortality rates are lower for married women than for widows, but the latter have a significantly higher rate for cancer of

TABLE II.—ENGLAND AND WALES, 1930–1932. MORTALITY FROM CANCER, BILIARY SYSTEM

Age	25—	35—	45—	55—	65—	70—
			1. Number of deaths			
Spinsters	12	38	108	175	121	280
Married	28	121	447	930	515	704
Widows and divorced		11	70	345	443	1639
			2. Mortality per 100,000			
Spinsters	0.4	2.2	8.3	19±1.4	37±3.3	62±3.7
Married	0.4	1.8	7.8	25.5 } 25.7±0.7	54 } 55±1.7	91 } 92±2.7
Widows and divorced		2.3	7.6	26.1 }	56 }	93 }

TABLE III.—ENGLAND AND WALES, 1930–1932. MORTALITY FROM CANCER OF SMALL INTESTINE, COLON AND OF PANCREAS, BY AGE AND MARITAL STATUS

Age	35—	45—	55—	65—	70—
		1. Number of deaths			
a. Spinsters Intestine	118	245	428	291	706
Pancreas	18	46	95	72	122
b. Married Intestine	333	925	1571	837	1240
Pancreas	62	197	404	185	219
c. Widows and divorced Intestine	28	225	793	856	3693
Pancreas	3	55	163	176	453
		2. Mortality per 100,000			
a. Spinsters	7.8	23.2	56.9	110.3	182.7
b. Married	5.9	19.6	54.3	106.8	189.2
a and b	6.3	20.2±0.5	54.8±1.1	107.6±2.9	186.8±3.9
c. Widows and divorced	6.9	30.6±1.8	72.3±2.3	130.3±4.0	234.6±3.6

the reproductive as well as for the accessible and inaccessible organs (Table V, Fig. 1).

CANCER ASSOCIATED WITH PREGNANCY AND/OR CHILDBIRTH

The frequency with which cancer appears in pregnant women is unknown. According to the gynecological literature, in 10,000 pregnant women 4 to 6 cases occurred. Provided this figure is correct, in England in 1931 the incidence should have been cancer in 252 to 378 women,[1] whereas according to age specific cancer rates for total population the expectancy should have been only 141.7 such cases.

[1]632,000 births were registered.

Yet according to the Registrar General in 1931 there were reported 14 cases and, in the 10 year period 1926–1935, there were altogether 113 cancer deaths associated with pregnancy or childbirth. Taking these figures at their face value, the conclusion may be drawn from the gynecological reports that the association of cancer with pregnancy is about 1.8 to 2.6 times the expectation, while from mortality statistics the figure is only $1/12$ of the expectation.

As the duration of illness due to fatal cancer is on the average 2 to 3 years, and as the duration of pregnancy including the puerperium is only about 10 months, the associ-

TABLE IV.—ENGLAND AND WALES, 1930–1932. MORTALITY PER 100,000 WOMEN BY AGE AND MARITAL STATUS

Age	35—	45—	55—	65—	70—
1. Biliary system, pancreas, small and large intestine (without rectum)					
a. Spinsters	10.1	31.5	76	147	245
b. Married	7.7	27.4	80	160.5	280.5
c. a and b	8.2	28.1±0.6	79.0±1.3	157±3.4	267±4.6
d. Widows and divorced	9.2	38.2±2.0	98.4±2.7	186±4.8	328±4.3
2. All other "inaccessible" organs*					
a. Spinsters	11.1	34.5	73.8	119	182
b. Married	10.8	30	73.4	114	177
c. a and b	10.9±0.4	31.3±0.6	73.5±1.2	116±2.9	179±3.8
d. Widows and divorced	7.6±1.2	29.8±1.8	70.6±2.2	112±3.7	166±3.0

*Rectum, intestine undefined, peritoneum, omentum, mesentery, anus, larynx, lung, mediastinum, brain, thyroid, kidney, bladder, bones, jaw excepted, and "others."

TABLE V.—ENGLAND AND WALES, 1930–1932. ALL CANCER DEATHS BY AGE, MARITAL STATUS

Age	25—	35—	45—	55—	65—	70—
1. Number of deaths						
Spinsters	415	1,177	2,830	3,828	2,090	4,353
Married	1,119	4,978	11,514	14,602	6,122	7,418
Widows and divorced	20	424	2,254	5,979	5,464	19,154
2. Deaths per 100,000						
Spinsters	12.6±0.6	68±2.0	219±4.1	416±6.7	635±13.1	961±14.5
Married	16.9±0.5	75±1.0	202±1.9	401±3.3	639± 8.1	962±11.2
Widows and divorced	16.1±3.6	89±3.9	246±5.1	452.3±5.8	692± 9.3	1084± 7.8

ation of cancer with pregnancy and childbirth should be 2.4 to 3.6 times as frequent as that of the actually reported cancer deaths. The 14 fatalities from cancers reported in 1931 would therefore indicate an association of cancer with pregnancy about 3 times greater, i.e., 42 cases, or 0.66 times in 10,000 pregnant women. The association of cancer and pregnancy reported by clinicians is 6 to 9 times higher than this figure.

The association of pregnancy and cancer is more probable at the beginning of the illness than in the later stages. Hence, the mortality reports underestimate the likelihood of occurrence while clinical reports overestimate it as pregnant women suffering from cancer are more likely to attend the hospital than the average pregnant women.

As to the age factor in the occurrence of cancer deaths during pregnancy or at childbirth, the difference is smallest in the age group below 24 years, it is higher between 25 and 44 years of age, and is at its peak in the age group between 35 and 44. The difference seems therefore to increase as age advances[1] and as the pregnancies increase (Table VI).

PARTURIENT HISTORY AND CANCER BY SITE

Cancer of the gall bladder is correlated with the parturient history; therefore, the figures brought out here are not surprising. The explanation of the other findings is less easy. According to former studies, the primary tumor as far as it depends upon the parturient history, may be located in the uterus, the

[1] No calculations could be made for the age group 45 to 49.

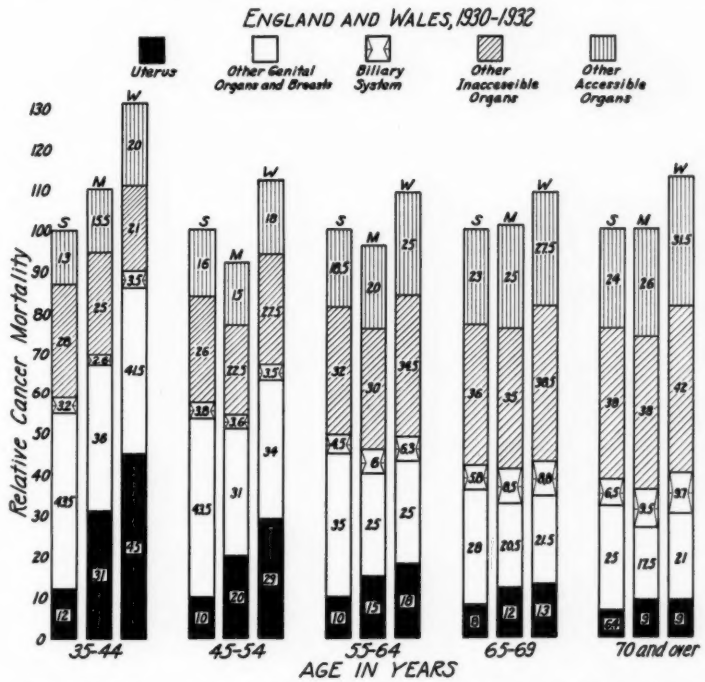


Fig. 1. Relative cancer mortality by site, age, and marital status in single (S), married (M), and widowed (W) women in England and Wales (1930–1932).

ovaries, the breast, and the gall bladder as well as in the stomach. It is not located in the intestines, however. In the total cases of cancer arising in the gastro-intestinal tract, in the biliary system, and in the reproductive organs, only those of the intestinal tract are not correlated with reproductive activity. There are, of course, no official mortality statistics which divide cancer victims according to their parturient history. Such data, however, may be obtained from representative clinical material and applied to official mortality statistics, which show the distribution of cancer by site in the female. I made a study of the pregnancy histories of 2,927 women above 45 years of age (Vienna University Clinics), 1,725 of them were suffering from cancer of the genital organs, 423 from breast cancer, 403 from cancer of the stomach, 280 from intestinal cancer, and 96 from cancer of the gall bladder. I applied the pregnancy data to the 1,395 women over 45 years old who died during 1928 in Vienna of cancer of one of these organs. Thus I estimated among deaths from cancer in the entire population the number of nulligravidæ, of women with 1 to 3, with 4 to 7, and with 8 and more pregnancies. As shown in Table VII, when the cases are grouped according to the woman's parturient history the distribution of the primary malignancies varies. However, the ratio as to intestinal cancers remains almost unchanged, that is 17.7 per cent in the nulligravidæ and 18.3 per cent in women with more than 7 deliveries (Table VII).

While these figures are only a rough estimate, there is no other material published which gives these relations. Table VII complements the analysis of the English mortality statistics. It is probable that the differences in rates for widows and the other women as far as cancer of the colon is concerned are due neither to the parturient history

TABLE VI.—ENGLAND AND WALES. ACTUAL AND CALCULATED ASSOCIATION OF CANCER DEATH WITH PREGNANCY OR CHILDBIRTH BY AGE

Age	a/	b/	c/	d/	e/	f/	g/
	Birth rate per 1000 women (1931)	Cancer death rate per 1000 women (1926–1935)	Expected association of pregnancy and fatal cancer per 1 million women (a×b)	Actual association of pregnancy and cancer in 1926–1935			$\frac{c}{e}$
				Number of deaths reported			
				Per year	Per million women	Per thousand pregnant women	.. times
15–19	12.36	0.0302	0.3733±0.15	0.1	0.0579±0.06	0.0048±.0048	6.4
20–24	70.82	0.0433	3.0665±0.41	0.8	0.4456±0.16	0.0058±.0020	6.9
25–29	111.98	0.0880	9.8542±0.75	1.1	0.6366±0.12	0.0057±.0017	15.5
30–34	93.35	0.2315	21.6105±1.10	3.1	1.9112±0.34	0.0205±.0036	11.3
35–39	61.14	0.5109	31.2364±1.02	3.0	1.9800±0.36	0.0323±.0059	15.8
40–44	24.71	1.0053	24.8410±1.31	2.5	1.7455±0.35	0.0704±.0139	14.2

TABLE VII.—VIENNA, 1928. CANCER OF GENITAL ORGANS, BREAST, STOMACH, INTESTINES AND BILIARY SYSTEM IN WOMEN OVER 45 DIVIDED BY THE NUMBER OF PREGNANCIES*

Organ or part	0	1–3	4–7	8 and more
	Pregnancies			
	%	%	%	%
Cervix uteri	11.0	19.6	18.5	23.6
Other genital organs	22.0	12.8	8.9	6.7
Breast	17.8	13.0	10.4	8.4
Stomach	21.6	28.1	30.7	25.8
Biliary system	9.8	9.0	12.9	17.1
Intestines	17.7	17.4	18.3	18.3
	100	100	100	100

*1,395 fatal cancer cases.

and standard of life nor to diagnostic errors. They should be traced rather to the reactions of the body incident to the loss of the *pater familias*. This circumstance in the carcinorelevant mechanism remains to be clarified.

SUMMARY

1. Marital status. The total cancer mortality as well as the site of the primary tumor—genital organs, breast, stomach, biliary system, pancreas, and colon—is influenced by the marital status. During the age of reproduction married women show higher cancer rates than do spinsters; in the 20 years following there are small differences in favor of married women; above the age of 64 both groups have about equal cancer mortality rates. These cases differ from one another only in the distribution of the primary tumors. In widows the age specific mortality rates are higher for cancer of genital organs, breast, stomach, pancreas, and colon than in single or married women; widows also succumb more frequently to gall bladder cancer than do single women.

2. Reproductive activity. There is a correlation between reproductive activity and the changes in the cancer distribution within the genital organs, the breast, biliary system, and stomach, the incidence increasing in some organs and in others diminishing. These changes counterbalance each other.

3. Cancer and pregnancy. The simultaneous occurrence of cancer with pregnancy seems less frequent than would be expected, the deficit increasing as age advances, and as the average number of pregnancies increases.

REFERENCES

1. Bertillon, J. Internat. Cong. Hyg. & Demography, 1907, 3: 1335.
2. Peller, S. Ztschr. f. Krebsforsch., 1930, 30: 581.
3. Idem. Ztschr. f. Krebsforsch., 1931, 34: 394.
4. Idem. Human Biology, 1937, 9: 57.
5. Peller, S., and Stoehr. Ztschr. f. Krebsforsch., 1929, 28: 266.
6. Registrar—Generals Decennial Suppl., Eng. and Wales, 1921, Pt. 3a. London, 1928.
7. Ibid. 1931, Pt. 2a. London, 1938.
8. Stocks, P. J. Roy. Statist. Soc., 1938, 101: 669.

CLINICAL SURGERY

FROM SURGICAL CLINIC, PROFESSOR DR. JOSÉ ARCE, UNIVERSITY OF BUENOS AIRES

RHINOPLASTY

Argentine Method

Dr. OSCAR IVANISSEVICH and Dr. ROBERTO C. FERRARI,
Buenos Aires, Argentina

THE Argentine method described in 1921 by Dr. Oscar Ivanissevich employs the pinna with its skin and cartilage to repair loss of tissue in the soft parts of the nose, its tip and alæ. The pinna is transplanted by means of the thumb, as shown in Figures 1 to 13. Since 1921 the author and his collaborators have used this method 46 times. In Lima, Peru, Professor Fortunato Quesada operated upon 2 patients successfully and reports of these cases have been published.

Tissue from the ear has been chosen because of its similarity to the tissues of the soft part of the nose. The cartilaginous structure gives elasticity and toughness to the graft. The graft is so constructed that the skin of the mastoid area is used to cover the apex and the alæ. The skin of the outside part of the ear is used to form the nasal vestibule. The convex end of the helix, therefore, faces downward and outward.

The technique used in the transplantation resembles that of the Italian method and is carried out in two stages. In the first stage (Fig. 4) the pinna is sutured to the fleshy part of the thumb. This has to be done very carefully and in two planes. In the deep plane the periosteum of the third phalanx is fastened with thin catgut to the cartilage of the ear (Fig. 13). In the superficial plane the skin edges of the ear are carefully sutured with silk to the skin of the finger.

Ten days later the skin sutures are removed and the circulation from the ear to the finger is intermittently interrupted, by means of continuous pressure tongs. For the first few days pressure is exerted for only 5 minutes and then gradually the interruption period is increased until pressure is applied for an hour by the twentieth day. If the digito-auricular flap is large and cicatrization is normal, this period will be sufficient. When the graft does not change color upon interruption of the auricular circulation of blood, that is, when circulation in the graft has been established, then the propitious moment to sever the section from the ear has arrived.

In the second stage the pinna is divided at the level of the line upon which the continuous pres-

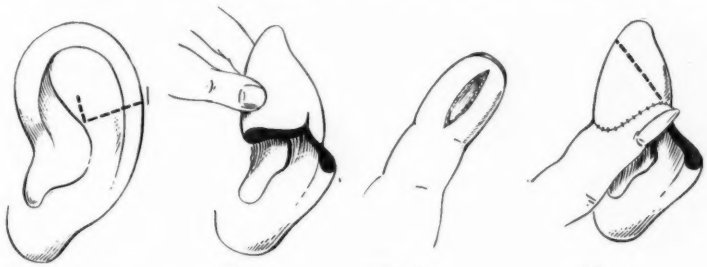


Fig. 1. Fig. 2. Fig. 3. Fig. 4.

Fig. 1. Outline of incision which is used for section of the auricle.
Fig. 2. Turning of the tube flap.
Fig. 3. Incision in fleshy part of thumb.
Fig. 4. Digito-auricular suture. The dotted line shows the line of future section.

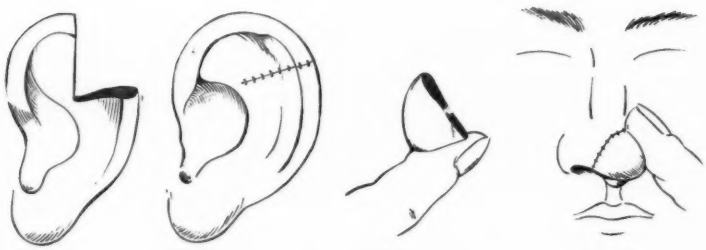
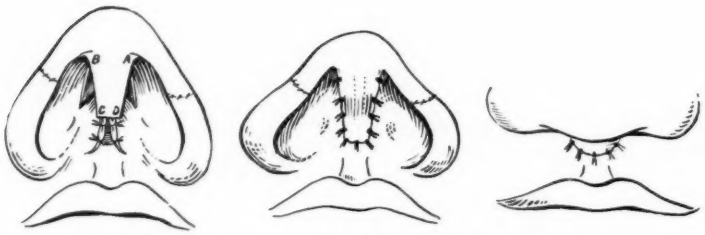


Fig. 5. Fig. 6. Fig. 7. Fig. 8.

Fig. 5. Defect in ear after removal of flap.
Fig. 6. Shape of ear after suture of defect.
Fig. 7. Thumb with section of ear attached
Fig. 8. The flap with finger still attached has been sutured to the nose.



Figs. 9, 10, and 11. Construction of the septum and the subseptum.

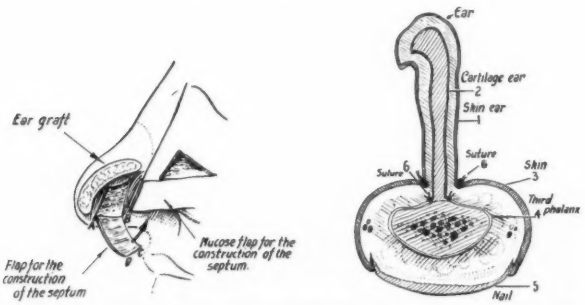


Fig. 12, left. Final steps in construction of the septum and subseptum.
Fig. 13. Sectional view of finger attached to ear.

sure tongs has been placed, and the finger with the piece of pinna attached is thus isolated (Fig. 7). It is now possible, depending upon circumstances, the age and tolerance of the patient, to proceed with the operation. The free end of the pinna flap may be sutured and cicatrization waited for, or the second stage may be done immediately, that is the piece of ear attached to the finger may be fixed to the nose. The surgeon must decide what is best in the particular case.

Suture of the auricular flap to the nose after the stump is freshened is very easy and yet requires special care (Fig. 8). The suturing must be done in three planes: in the cutaneous plane of vestibule, the cartilaginous plane, and in an external cutaneous plane. The last suture is intradermic.

From the tenth day on interruption of circulation with the tongs is again carried out. Usually it is possible to separate the finger from the graft after 20 days.

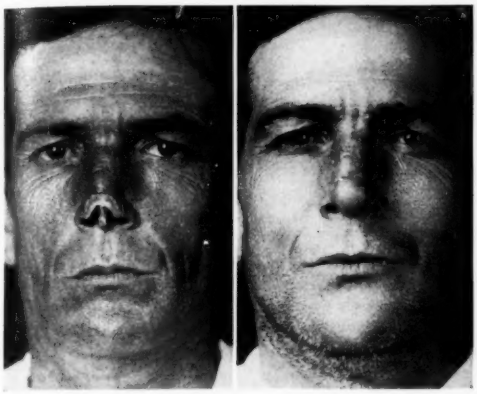


Fig. 14, left. Cancer of the nose healed by radium.
Fig. 15. Ivanissevich graft has been applied.

Fig. 16. Section of ear attached to finger ready for application to nose.

After the finger is freed the surgeon may decide to join the free end of the graft to the nasal stump immediately or he may suture the free end and wait until cicatrization is complete. The decision depends upon the nutritional condition of the graft. Occasionally during this process as well as during the earlier stage of the operation, the skin of the graft may become edematous and brittle. In such cases it is best to act with caution and, before proceeding with the next stage, to wait beyond the 20 day period mentioned for both stages or until epidermization of the graft is complete.

The third stage consists in the final adaptation of the graft. No special description of technique is needed. The prime essential is great care in the suture which is best done in three layers.

The subseptum can be made from the skin of the inferior face of the auricular graft. On this skin a cutaneous trapezoidal flap of the inferior base is carved as shown in Figures 9, 10, 11, and 12. The skin is dissected up to the cartilage and the ends are sutured to the remaining piece of the nasal septum.

In some cases it is necessary to make some finishing touches, and in others complementary grafts are necessary.

Immobilization apparatus. The apparatus which we have used consists fundamentally of a leather glove which encloses the hand and wrist, and a set of ribbons which make it possible to fix the thumb in the best position in any of the stages during the process of digito-auricular suture and during the process of digital, auricular-nasal suture. Quesada has used an improvised apparatus of court plaster but we do not recommend it. It is necessary that the apparatus be very firm so that displacements are reduced to a minimum. During the second stage the auricular-nasal suture, to insure immobilization of the thumb in restless patients we make a perforation in the free part of the nail and with a strong string we tie the nail to the head bandage. During the first few days the patient naturally suffers from the immobilization but he soon is relieved and is able to perform easy movements with the free fingers and massaging of the shoulder, the elbow and the forearm. Some patients can get up from bed and walk without any difficulty. In 2 cases the pa-

Figs. 17 and 18. Front and lateral views of reconstructed nose shows perfect result.

tients left the hospital the day of operation and went home. The personal factor here as in any other type of surgery is very important. In only one case did the graft become separated in the second stage but it could be sutured successfully again in 1 month.

Repair of the ear. The repair of the ear is simple when only a small amount of tissue is removed, but a real operation is required when a large amount of tissue is removed. In the former case direct suture is sufficient for reconstruction of the pinna; the ear appears smaller but is of natural form. If the amount of tissue removed is large, repair may be accomplished by means of an autoplastic operation with skin from the mastoidal region or with a tubular graft.

GENERAL RESULTS

Up to the present time we are unable to find reported results better than ours, no matter what method has been used. The Argentine method has already stood the test of time. Our first patient was operated upon 20 years ago. Photographs show not only the immediate result but the condition 20 years later.

Our experience in 46 cases makes it possible to speak with authority as to the merits of this method and to state that it gives the best results in the shortest time.

BIBLIOGRAPHY

1. Arana, Guillermo Bosch. Técnica quirúgica sincronizada. 1938, 1: 565.
2. Christman, Federico E., Ottolenghi, Carlos L., Von Grolman, Juan Manuel Raffo y Gunther. Tratado de técnica quirúrgica, Buenos Aires, 1929, 1: 336.
3. Fomon, Samuel. The Surgery of Injury and Plastic Repair, p. 797. Baltimore, 1939.
4. Hunt, Harold. Plastic Surgery of the Head, Face, and Neck, p. 227. Philadelphia and New York: Lea & Febiger, 1926.
5. Ivanissevich, Oscar. El método argentino para la rinoplastia. Prensa méd. argentina, 1921, July 30.
6. Idem. A new method for rhinoplasty. Surg., Gynec. & Obst., 1923, 36: 828–829.
7. Ivanissevich, Oscar, and Ferrari, Roberto C. Tres nuevos casos de rinoplastia por el método argentino. Bol. d. inst. de clín. quir., 1927, No. 20, p. 103.
8. Idem. La reconstrucción del ala nasal por el método argentino. Semana méd., 1930, No. 16, p. 967; Bol. d. inst. de clín. quir., 1929, No. 43, p. 19.
9. Limberg, A. R. Reconstrucción de la punta, alas y paredes nasales por injerto auricular sobre tallo redondo; técnica de Vechmotor y de Ivanissevich, 1925. Vestnik Hirurgi i prograničnii oblesti Kniga pedeset peta. Leningrado, 1930.
10. Quesada, Fortunato. Rinoplastias en tres casos personales; método de Ivanissevich. Colaboración del Perú. El Día Médico, 1931, Aug. 3.
11. Rubatto, Guillermo. Rinoplastia por el método de Ivanissevich. Thesis, Faculty of Medicine of Lima, 1927.

THE OPENING OF THE ANTERIOR TRACHEAL WALL IN TRACHEOTOMY

RICHARD WALDAPFEL, M.D., Grand Junction, Colorado

TRACHEOTOMY is one of the oldest and most important of the surgical procedures and belongs to the general category of neck operations. It is not limited to any one specialty and should be mastered by the laryngologist, surgeon, and general practitioner. In spite of its being an old operation, failures still occur during the course of the operation and in the after-treatment. Some of these are due to the method of opening the trachea itself.

Historical evidence shows that the method of opening the trachea has varied from time to time. During former centuries operations involving incisions in the cartilages of the trachea were shunned because such a procedure was regarded as dangerous. Incisions were made instead between the cartilages through the intercartilaginous ligaments (Kuehn).

During the nineteenth century the so-called "classic method" came into favor. In this operation after exposure of the trachea below the cricoid cartilage, a longitudinal incision is made in the anterior tracheal wall through several cartilaginous tracheal rings and intercartilaginous ligaments. The incision is then pulled apart by small retractors or spread apart by a dilator and a cannula is inserted into the trachea through this opening. This became the operation of choice and the technique is still presented in many surgical and laryngological textbooks.

By this method, parts of the cartilaginous tracheal rings are spread apart, bent upon themselves and buckled in an unnatural position in order to furnish room for the cannula. The evils that result may complicate the healing of the wound and the process of decannulization. The principal objections to this method are:

1. The C shaped cartilaginous rings, which are open at the back and connected there only by the membranous wall of the trachea, are dislocated by the cannula. The pressure causes the soft membranous wall of the trachea to bulge forward toward the lumen of the trachea thus making it narrower (Fig. 1b).

2. The cut edges of the elastic cartilaginous rings in front are bent by the pressure of the tube and the frequent change of tube may result in a narrowing of the tracheal lumen (Fig. 1d).

3. The cut edge of the split cartilaginous rings on which the tube is continuously rubbing undergoes inflammatory changes and becomes covered with granulations. The cartilage around the tube becomes soft, is easily destroyed, and later is replaced by connective and scar tissue. This latter tissue may contribute to the formation of stenosis. Even if no stenosis results, the anterior wall of the trachea may lose its cartilaginous support and, after removal of the tube, move in and out with each inspiration and expiration.

These disadvantages will be of a temporary nature and subside if the tube lies in position only for a short time. They become definite conditions if the tube is worn for a period of time with proliferation of connective and scar tissue. In addition there are minor difficulties when the tube is changed. The slit in the trachea lies at the bottom of a long funnel shaped wound and is accessible only with difficulty. Often the change of tube is liable to become an exciting experience for both the doctor and the patient.

Since the middle of the past century attempts have been made to eliminate the disadvantages of the slit incision method. Marshall Hall in England and Dieffenbach in Germany made the first fundamental change in the method by making, instead of the simple incision, an *excision* of a part of the anterior wall of the trachea. After opening the trachea, Marshall Hall introduced a piece of cork into it and used this as an underlying support; then with an iron punch and mallet he removed a round piece of the trachea. Dieffenbach removed a square piece of trachea amounting to two cartilaginous rings. American physicians, See and Donkoff at about the same time, tried to overcome the evils of pressure from the tube by cutting an opening into the anterior wall of the trachea and placing a silver wire in it.

It is interesting to note that while the excision method, though devised by leading surgeons of their respective countries, has not been given much consideration by surgeons, it has been accepted and improved by European laryngologists. Thost made it the method of choice and

Presented at the Pacific Coast Eye, Ear, Nose and Throat Meeting, San Francisco, California, June 20, 1939.

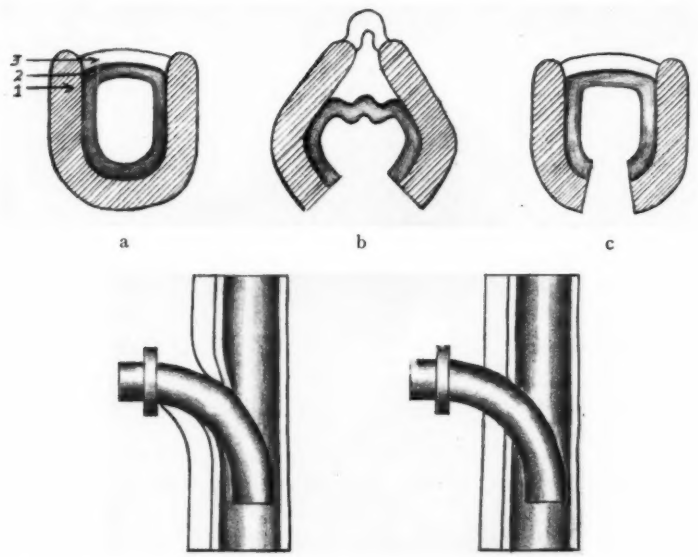


Fig. 1. Transverse and longitudinal section of the trachea. (Modified from Thost.) a, Normal trachea: *1*, cartilage; *2*, mucous membrane; *3*, posterior wall. b, Trachea after incision of anterior wall; note buckling of posterior wall. c, Trachea after excision of anterior wall; note posterior wall smooth. d, Tube inserted after incision; note dislocation of anterior tracheal wall. e, Tube inserted after excision; note undisturbed anterior wall.

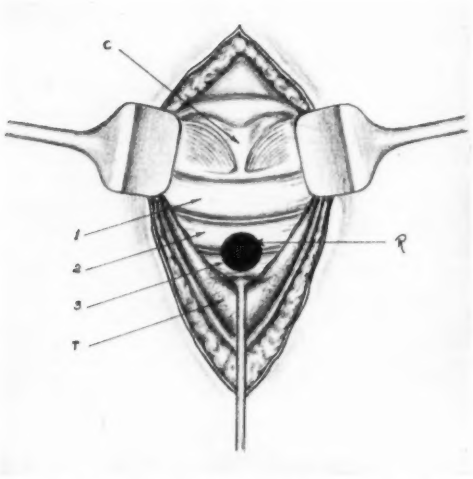


Fig. 2. Tracheotomy with window resection in the anterior wall. *C*, Cricoid; *1*, *2*, *3*, first, second, and third rings of trachea; *T*, isthmus of thyroid gland; *R*, resected part of anterior wall.

the Viennese school of laryngology (Hajek and his immediate predecessors) used it advantageously.

It is obvious that laryngologists appreciated the great advantage of this method more than did surgeons. They observed, more diligently perhaps, the patients who wore the tubes over longer periods of time; they noticed the damage that was done by the tube and recognized the causes producing the damage and made attempts to avoid them.

They believed that pressure from the tube and displacement of the tracheal cartilages were the main causes of damage, and they observed that *excision* of a portion of the tracheal wall rather than a simple *incision* was far more satisfactory. This postulation had a sound mechanical basis. No plumber working with metal or rubber tubing would consider making a union or inserting a connection through a slit in the tube; they would cut a hole for the connection. This means that in a tracheotomy the *incision* must be replaced by an *excision*. A window is cut in the anterior wall of the trachea of sufficient size to accommodate the

tube to be inserted (Fig. 2). When the tube is introduced the cartilages are not spread apart, not bulged forward from behind, nor pressed upon too much (Fig. 1c). Neither destruction of, nor granulations on, the tracheal cartilages occurs. Long years of experience have shown that resection of the piece from the anterior wall is harmless as regards later functioning of the trachea.

The use of resection facilitates considerably the after-treatment and change of the tube. The permanent opening usually makes dilatation a superfluous measure. The level of the opening is of minor importance if one fundamental rule is observed, namely: the cricoid cartilage must not be injured and under no circumstances must it be exposed to the pressure from the tube.

The resection is performed customarily with forceps and small bent scissors. If there is ossification of the cartilage this may be quite difficult. Also if one does not perform a tracheotomy frequently some difficulty may be encountered in cutting out just the right amount to accommodate the tube. The opening should be made as sharp edged as possible; the cartilage and the tracheal mucous membrane should be cut out precisely and sharply.

To overcome these difficulties and to perform the resection more easily, I have devised an instrument, the manipulation of which is simple. It has proved satisfactory in many tracheotomies (Fig. 3). Without difficulty the instrument cuts the hardest rings together with the adherent perichondrium and mucous membrane. The instrument makes the opening of proper size, clean and sharp edged, and automatically prevents the aspiration into the bronchi, of the excised piece of tracheal wall as it holds the piece intact until removed. The principle embodied in the instrument is the result of many years of experience in this field of surgery. It has recently been modified so that it will fit the American universal handle.[1]

The resection thus is performed simply in the following way:

After exposure of the trachea the membranous annular ligament between the second and third tracheal rings is split transversely, the disc of the instrument is introduced into the slit, and the instrument is closed as is a conductor's punch. It is removed and the excised piece of tracheal wall is contained therein. By the opening thus produced the tube is passed easily into the trachea. The entire procedure could not be simpler.

[1]The instrument is manufactured by V. Mueller and Company.

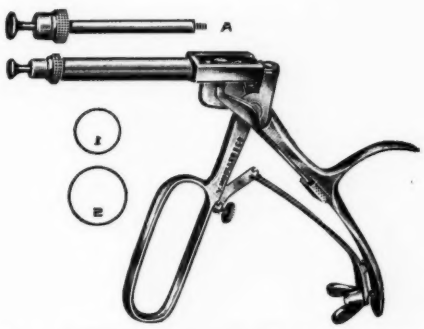


Fig. 3. Instrument for performing the window resection in tracheotomy. Exchangeable tip *A* showing variation in size for different age as is also depicted in the openings *1* and *2* for a child and for an adult. The instrument with tips is approximately one-third natural size, *1* and *2* openings are normal size.

It is the purpose of this discussion to present a method of performing tracheotomy which has proved satisfactory, and which avoids a number of rather untoward consequences. I believe the method can be recommended wholeheartedly.

BIBLIOGRAPHY

1. HAJEK, M. The Diseases of the Larynx and of the Trachea. Leipzig: C. Kabitzch, 1932.
2. HALL, MARSHALL, and DIEFFENBACH. Quoted from Bardeleben's Chirurgische Operationslehre. Leipzig, 1872.
3. KUEHN, J. The Artificial Opening of the Upper Airways. Reprint from Guenther's Operationslehre. Leipzig and Heidelberg, 1864.
4. SEE and DONKOFF. Quoted from Sargnon's Tubage et tracheotomie en dehors du croup. Paris: Bailliére et fils, 1900.
5. THOST, A. The Stenoses of the Upper Air Passages Following Tracheotomy and Their Treatment. Wiesbaden: J. F. Bergmann, 1911.

BILATERAL INTERCOSTAL NERVE BLOCK FOR UPPER ABDOMINAL SURGERY

ROBERT W. BARTLETT, M.D., St. Louis, Missouri

A VITAL problem confronting the surgeon daily concerns the proper choice of anesthesia for each individual case since every one of the numerous anesthetic agents and methods ordinarily employed possesses qualities which limit its usefulness.

Our own dissatisfaction with methods of anesthesia available to us for operations on certain seriously ill, jaundiced patients was the original stimulus for this study, but as we have gone further with bilateral intercostal nerve block its usefulness has been found to cover a wide range in intra-abdominal and abdominal wall surgery.

But to return to the jaundiced patient requiring surgery, we have tried whenever possible to avoid an ether anesthesia since by this method an additional load is thrown on a liver and kidneys already damaged. This, then, has meant that spinal was probably the anesthetic of choice in these cases. However, certain of these patients may present some of the standard contra-indications to spinal anesthesia, such as marked anemia or extremes of blood pressure, which preclude its use. Then, too, if one is unfortunate enough to have a severe reaction follow the use of spinal anesthesia in an already seriously ill patient, the outcome may be disastrous. It is thus apparent that spinal anesthesia will often be unsuitable. Cyclopropane is proving to have a wide range of usefulness, but when employed in concentrations sufficient to produce the degree of muscular relaxation usually necessary for work on the common duct, the definite hazard of serious depression of vital functions exists.

Paravertebral nerve block anesthesia has never gained any considerable popularity because of the technical difficulties inherent in the method, the result being a failure to obtain proper anesthesia in too large a percentage of cases. The reader is referred to Hertzler for illuminating comments both on paravertebral and splanchnic anesthesia. In recent years Dogliotti and Odum (8, 9) have advocated epidural anesthesia for patients not suitable for spinal or general anesthesia, but here again, to quote the latter author, "The skill and care necessary for administration of an epidural anesthetic, coupled with the fact that one must wait 15 to 20 minutes for the onset of anesthesia, makes it probable that epidural anesthesia will not be used in busy hospital services."

It occurred to us that our problem could be solved by blocking the lower intercostal nerves in the midaxillary line so that their lateral branches could be included along with their anterior branches and thus would be obtained complete anesthesia of the anterior and lateral abdominal wall including the parietal peritoneum from the costal margin to approximately 2 inches below the umbilicus. In as much as sensation to the visceral peritoneum is by way of the splanchnics a light gas anesthesia must be given in conjunction with the nerve block during the intra-abdominal part of the operation in order that ordinary handling and packing off of intestines may be performed without pain to the patient and to this we have found no objection. In the past for operations in the upper abdomen it has been rather common practice to block the nerves by infiltrating along the costal margin and down the lateral border of the rectus muscle. The method we propose has several distinct advantages over the one just referred to due to the fact that the lateral flat abdominal muscles, namely, the external oblique, internal oblique, and the transversus abdominis are paralyzed as likewise is the periphery of the diaphragm. As a result the ability of the patient to strain, as occurs during marked respiratory effort or vomiting, is minimized so that there is little tendency of the intestines to be pushed out of the wound during operation. Second, accurate and rapid closure of the abdominal wall is obtained at the conclusion of the operation since the lateral muscles are paralyzed and not pulling the wound open as they do when only a circular infiltration about a rectus incision is performed. It is a corollary of this that postoperative hernia and eventrations are far less common when the peritoneum and posterior rectus sheath have been accurately approximated, thus avoiding defects into which the omentum can work its way. This kind of closure, of course, is possible only in the completely relaxed patient.

It is apparent, therefore, that by means of a perfectly simple method of anesthesia we are able to

From the Department of Surgery, Washington University School of Medicine.

enjoy the advantages of a full ether or spinal anesthesia in the care of patients presenting definite contra-indications to those methods. As stated earlier in this paper, we were originally interested in obtaining a safer anesthesia for certain extremely sick jaundiced patients, but as time has gone on we have extended its use to include almost any surgical procedure required in the upper abdomen, also any work on the abdominal wall from about 2 inches below the umbilicus up to the costal margin. In this latter instance one may or may not, as one wishes, administer gas for 3 to 5 minutes while the intercostal injections are being made, then stop the inhalation and carry out the plastic procedure on the wall under the ensuing nerve block. We have been particularly pleased with the ease of repairing umbilical and incisional hernias and of closing colostomies in the transverse colon by this method in cases in which it seemed wise to avoid the possibility of a reaction to spinal anesthesia.

I recall a particular instance of eventration in which the method was perhaps life-saving. A husky, 6-foot, young adult male had been subjected to exploration through an upper right rectus incision for a stab wound of the liver following which he developed lobar pneumonia and the wound broke open on the fifth postoperative day, probably as a result of severe coughing. Bilateral intercostal nerve block was carried out after the skin was infiltrated, and, with the patient in bed in his own room, the wound was closed without difficulty by means of through-and-through silkworm gut stay sutures. Following this the patient recovered from the pneumonia and the abdominal wall healed solidly.

The following operations have been performed under this method of anesthesia: exploration of common duct, cholecystectomy, cholecystostomy, cholecystogastrostomy, biopsy of liver, aspiration of liver abscess, closure of perforated typhoid ulcer, repair of incisional hernia, repair of umbilical hernia, closure of transverse colostomy, and secondary closure of abdomen after eventration.

We have had no failures to obtain anesthesia since the tissue planes through which the intercostal nerves pass are so very accessible in the midaxillary line for blocking; further, we know that we can expect at least an hour and a half anesthesia according to the technique to be outlined since we did, on one occasion, require that much time for exploring a common duct and repairing an incisional hernia, the result of a previous operation elsewhere.

A thorough search of the literature, including standard textbooks on anesthesia such as those of

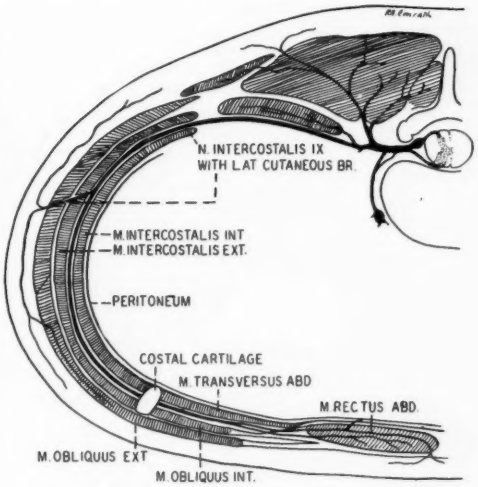


Fig. 1. Typical distribution of a lower intercostal nerve to the abdominal wall.

Labat, Hertzler, Farr, Gwathmey, and Flagg, discloses no plan of anesthesia for upper abdominal surgery bearing any very close similarity to the one we are proposing though many thoracic operations have been performed under intercostal block. Farr, in one of the many case reports in his book, simply makes the statement that a gastric resection was carried out under unilateral intercostal block in the nipple line from the fifth rib downward combined with transverse infiltration across the recti with a vertical limb in the midline plus anterior splanchnic anesthesia after the abdomen had been opened.

ANATOMY

According to Gray, the intercostal nerves pass forward (Fig. 1) in the intercostal spaces below the intercostal vessels. At the back of the chest they lie between the pleura and the posterior intercostal membranes, but soon pierce the latter and run between the two intercostal muscles as far as the middle of the rib. They then enter the substance of the internal intercostals and run amidst their fibers as far as the costal cartilages. The seventh, eighth, ninth, tenth, and eleventh intercostal nerves then pass behind the costal cartilages and between the internal oblique and transversus abdominis to reach the sheath of the rectus abdominis which they perforate. They supply the rectus abdominis and end as the anterior cutaneous branches of the abdomen; they supply the intercostal and abdominal muscles. About

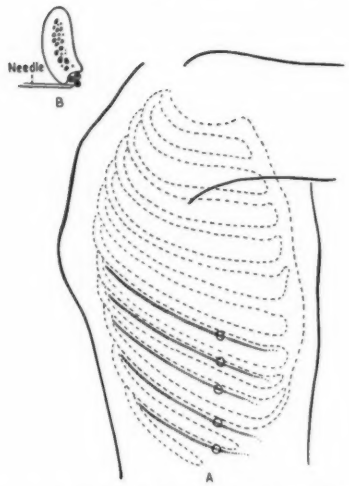


Fig. 2. A, Sites of injection of seventh, eighth, ninth, tenth, and eleventh intercostal nerves in midaxillary line. B, Nerve lying at inferior border of rib between external and internal intercostal muscles.

the middle of their course they give off lateral cutaneous branches. These pierce the external intercostals and the external abdominal oblique and divide into anterior and posterior branches which distribute to the skin of the abdomen and back; the anterior branches supply the digitations of the external abdominal oblique and extend forward and downward nearly as far as the margin of the rectus abdominis; the posterior branches pass backward to supply the skin over the latissimus dorsi.

Thus it is apparent that the site of election for injection of the anesthetic agent is in approximately the midaxillary line where the nerve, lying at the lower border of the rib and between the two intercostal muscles, is most easily accessible and where the lateral cutaneous branch of the nerve supplying most of the external abdominal oblique muscle will be included in the block.

TECHNIQUE OF ANESTHESIA

Modern practice presupposes that the patient will arrive at the operating suite with an adequate basal anesthesia. Ethylene or any other suitable gas is then administered for 2 or 3 minutes so that the patient will not be aware of the ensuing needle pricks. During this time the arms may be abducted and the skin of the lateral chest wall on either side prepared from the level of the nipple to below the costal margin.

In view of the fact that one should allow approximately 10 minutes for any nerve block anesthesia to become effective it has been our custom to don sterile gloves and do the injections, then scrub while the anesthetic is taking hold, thus wasting no time.

We have been employing 2 per cent novocain solution with 3 minims of adrenalin to the ounce added in order to insure sufficient duration of anesthesia. As stated earlier, we have not required more than an hour and a half thus far; however, should one foresee the probability of a more prolonged operation there are several longer-acting drugs available for injection.

The seventh, eighth, ninth, tenth, and eleventh intercostal nerves on each side are blocked in the midaxillary line (Fig. 2) starting from the lowest one and working upward. We use any suitable syringe and a No. 17 caliber needle with a point sufficiently blunt so that its passage through a fascia layer can be appreciated. We palpate the lower border of the rib and then the needle is passed through the skin and fat down to this point. Following this the needle is allowed to slip off the lower border of the rib. In so doing it is easily felt to pass through the fascia covering the external intercostal muscle. The needle point now lies between the two intercostal muscles at the costal groove where run the intercostal vessels and nerve. The injection of between 3 and 4 cubic centimeters of the anesthetic solution is quite sufficient for each nerve; thus with 5 sites of injection on each side a maximum of 40 cubic centimeters is employed.

If one person performs the bilateral block, about the same time is required as for administering a spinal anesthesia; however, if the surgeon and his first assistant each do a side simultaneously, a matter of only 2 or 3 minutes is involved in this procedure.

As stated earlier, a light gas anesthesia must be maintained during the intra-abdominal portion of the operation in order that intestines may be handled and packed off without pain and shock to the patient; however, when one is closing the abdomen or performing a plastic operation on the wall, such as repair of umbilical or incisional hernia, the gas may be dispensed with as soon as the nerve block has become effective. As an alternative method, the block may be performed under "local" instead of gas if the operation is to be confined to the abdominal wall; then, too, there may be some who will wish to combine this block with anterior splanchnic anesthesia in preference to gas for intra-abdominal operations. We have had no experience with splanchnic anesthesia.

SUMMARY

Bilateral block of the seventh through the eleventh intercostal nerves in the midaxillary line combined with light gas inhalation constitutes an extremely safe and satisfactory anesthesia for upper abdominal operations on certain seriously ill patients presenting contra-indications both to ether and spinal anesthesia.

It possesses all of the virtues of spinal anesthesia, such as complete relaxation and absence of pushing of intestines without any of the dangers sometimes associated with its use. Because of the relaxation, closure is rapid and the operation accordingly shorter. By the same token, approximation of the posterior rectus sheath and peritoneum is accurate and thus an important factor in the development of postoperative hernia is eliminated.

For plastic procedures on the upper two-thirds of the abdominal wall such as repair of umbilical and incisional hernias, secondary closure subsequent to eventration, and closure of colostomy in the transverse colon it has proved most useful.

The technique of injection is so simple that failure to obtain anesthesia should be rare. The time required for administration of the anesthesia is no longer than that involved in giving a spinal anesthesia and the duration obtained is sufficient for the completion of any operation one is apt to be required to perform in the upper abdomen or upon its wall.

BIBLIOGRAPHY

1. Dogliotti, A. M. Segmental peridural spinal anæsthesia. Am. J. Surg., 1933, 107: 118.
2. Farr, R. E. Practical Local Anesthesia. Philadelphia: Lea & Febiger Co., 1923.
3. Flagg, P. J. The Art of Anæsthesia. 6th ed. Philadelphia: J. B. Lippincott Co., 1939.
4. Gray's Anatomy. 1936, 23d ed., p. 938.
5. Gwathmey, J. T. Anæsthesia. 2d ed. New York: The Macmillan Co., 1924.
6. Hertzler, A. E. Technic of Local Anesthesia. 5th ed. St. Louis: C. V. Mosby Co., 1933.
7. Labat, Gaston. Regional Anesthesia. Philadelphia: W. B. Saunders Co., 1924.
8. Odum, C. B. Epidural anæsthesia. Am. J. Surg., 1936, 34: 547–558.
9. Idem. Recent advances in block anæsthesia. South. M. J., 1938, 31: 778–783.

SLIPPING OF THE UPPER FEMORAL EPIPHYSIS

Dr. HENNING WALDENSTRÖM, Stockholm, Sweden

SLIPPING of the upper femoral epiphysis is no longer regarded as a fracture; it does not depend for its origin upon trauma. Instead, the prerequisite is deficient bone formation between the epiphyseal cartilage and the metaphysis (collum). Due to this defect, the newly formed cells do not hold firmly enough together to be able to resist the pressure normally exerted on the head of the femur. The result is a displacement in the actual zone of ossification; that is, between the metaphysis and the epiphyseal cartilage, so that the epiphysis is displaced downward and backward in relation to the metaphysis. This softening process is transitory and, when it is at an end, the epiphysis ceases to slip and becomes firmly fixed in its new place. The deformity following displacement of the epiphysis is known as coxa vara and, in order to distinguish it from coxa vara of other origins, as epiphyseolytic coxa vara.

Before its real origin was known, the theory was that the deformity was the result of the femoral neck becoming curved; then it was called essential, static, or adolescent coxa vara. Distinction was made between this type of coxa vara, then considered to be the most common, and the type seen after epiphyseal slipping. This distinction was made probably because epiphyseal slipping was regarded more or less as a fracture, the direct result of trauma. We now know that epiphyseal slipping may be quite free of symptoms or at least cause so little trouble that medical care is not sought. In such cases the stages in the displacement are so closely spaced that one is tempted to speak of the condition as a continuous displacement of the epiphysis. Thus the only difference, either pathological or roentgenographic, between what used to be called essential coxa vara and the final stage of an epiphyseal separation is the manner of the slipping. In the former it proceeds slowly and almost imperceptibly and in the latter rapidly and is accompanied by more or less pronounced discomfort. The fundamental cause of the primary weakening of the metaphysis is not known, but there is strong evidence that it is to be sought in the disturbance of internal secretion during puberty.

From the Karolinska Institutets Orthopedic Clinic.

On the invitation of the University of Liverpool the author delivered this lecture as the Lady Jones Memorial Lecture on March 9, 1939.

For a better understanding of these problems, it is important to know the rate of incidence of epiphyseolysis in relation to other complaints. Hence I shall give a comparison based on figures obtained in Sweden.

The number of patients treated at orthopedic hospitals between 1932 and 1937, was 16,001. There were 184 cases of coxa plana (Legg's disease), an incidence of 1.15 per cent; 111 cases of epiphyseolysis, an incidence of 0.70 per cent. Epiphyseolysis is, therefore, less common than coxa plana. However, it is of greater importance to recognize it early, since excellent results can then be obtained if it is treated correctly, which is more than can be said of coxa plana. The type of treatment generally used up to now for separation of the epiphysis has lead to much greater disability than has treatment for coxa plana.

The cause of epiphyseolysis seems to be of constitutional character; in about one-fifth of the cases it is bilateral and in about one-third of the cases signs are found of endocrine disturbance, obesity, undeveloped external genitalia, and stunted growth—a picture resembling dystrophia adiposogenitalis. However, this term really applies to those serious disturbances which are caused by tumors near the hypophysis and result in hypofunction of the gland from pressure. Therefore the mild and often transitory disturbances here in question should be called the adiposogenital type of dystrophy. The four points mentioned make it probable that epiphyseal slipping—apparently a local condition—is the result of disturbances in the internal secretions. Which of the endocrine glands is mainly involved we do not know, but we do know that the anterior lobe of the hypophysis controls endochondral ossification and that it and the sexual glands are closely interrelated. In order that the body may develop normally, co-operation between the various endocrine glands must be well balanced. The presence of the adiposogenital type of dystrophy is clear evidence that certain difficulties must be overcome before the functions of the various endocrine glands become adjusted to each other. Just as the adiposogenital type of dystrophy is a disturbance of temporary character, so is epiphyseal slipping also transitory. As already stated it occurs only at a certain age, that is, during the period of puberty. The length of time during which slipping

can appear may be determined by examining all the bilateral cases in which displacement occurred more than once and calculating the time elapsed from the first roentgenological symptom of the first displacement to the first symptom of the last displacement. One and a half years was the longest time in any of my cases. Usually the time was 1 year, and this period corresponds to that in the cases reported in the literature. But why should an endocrine disturbance be suspected when two-thirds of the patients appear to be normal with no signs of obesity or defective development of the genitals? It must be said in this connection that disturbances in internal secretion may exist without causing any external changes. Furthermore, some young people with epiphyseal slipping are very tall and thin for their age. In young people hypertrophy of the anterior lobe of the hypophysis causes gigantism and atrophy of the anterior lobe causes dwarfism and in both instances the anterior pituitary hormone influences the endochondral ossification. It is possible, therefore, that, in addition to stimulating or inhibiting growth, a hyperfunctioning or hypofunctioning gland may also cause weakening of the newly formed layer of bone next to the epiphyseal cartilage. No other disturbance which points directly to the hypophysis has been demonstrable. There might be some change in size which would be revealed on a roentgenogram of the sella turcica, but innumerable investigations have yielded no result in this respect. No disturbance in calcium or phosphorus metabolism is observed in diseases of the hypophysis or in epiphyseal slipping.

It is clear from the foregoing that a disturbance in internal secretions must be considered as a possible primary cause of epiphyseal slipping. Therefore, as the background of every such case we must assume that there is a stage during which the new bone is not normal, a certain period during which the newly formed layer is not sufficiently resistant. Theoretically this condition must exist, but has anyone ever seen it, or can it conceivably ever be seen by any of the methods now at our disposal? Of course, it is possible that this stage may be accompanied by special pathological changes, but this is not certain. The adiposogenital type shows no changes in the ossification of the epiphyseal line before the slipping, and only exceedingly few cases of this disease are complicated by epiphyseal slipping. Furthermore, it is impossible to know in advance which of them will be so complicated.

Examination of specimens from cases in which slipping is already in progress shows nothing which might be of assistance in explaining the nature of the complaint. All that is revealed is the typical picture of absorption and new bone and cartilage formation.

Some investigators state that roentgenograms taken early in the disease show what they call the "preslipping stage." Characteristic of this stage is said to be the finding of an epiphyseal line broader and less dense than normal. Close examination of such pictures reveals a condition resembling the very beginning of an epiphyseal displacement. That which has been interpreted as the preslipping stage constitutes the first signs of epiphyseal displacement. This question is discussed farther on.

Even if a hypothetical pituitary disturbance is the primary cause of epiphyseal slipping, it is conceivable that some other general organic disturbance might produce a change in enchondral ossification. Common rickets reduces the power of resistance of the newly formed bone but only bending of the softer tissue. In the hip this results in a softened metaphysis becoming curved, a coxa vara deformity. Rickets is no longer present when epiphyseal slipping appears. Hence ordinary rickets cannot cause typical epiphyseal displacement.

Brailsford, of Birmingham, however, has shown that an extremely rare disease called "renal rickets" may give rise to typical epiphyseal slipping. In such cases the defective calcification in the newly formed bone tissue resembles that in common rickets. The word "renal" is used because in most of the cases hitherto described the patients have all suffered from chronic disease of the kidneys, characterized mainly by increased residual nitrogen. Acidosis with consequent release of calcium salts in the newly formed bone tissue has been considered to be the cause of the condition. In his handbook *The Radiology of Bones and Joints*, London, 1935, Brailsford reports a case of typical slipping of the upper femoral epiphysis first on one side and then on the other in a patient affected with renal rickets. He has been kind enough to send me his original pictures and a detailed description of the case.

I have been able to follow 1 case of renal rickets which was described by Gordh in *Proceedings of the Northern Orthopedic Association at Its XIX Meeting in Stockholm 1938* in *Acta orthop. scand.* In this case important changes were noted in both hip joints. On one side there was a broad zone of decalcified bone. Despite this, the epiphysis did not become loosened during the year I observed the patient, although she continued to walk. The defective ossification in the other hip was localized in the epiphysis, which had become softened and squeezed together in a manner closely resembling that in coxa plana.

On the basis of Brailsford's hypothesis, that slipping of the epiphysis is due to renal rickets, I determined the residual nitrogen and the calcium and phosphorous content of the blood of 7 cases of recent epiphyseolysis which have come to my attention. All were normal in these respects, and none showed albumin in the urine or the usual signs of nephritis. Even though Brailsford's case is of great interest in so far as it demonstrates that the cause of slipping of the epiphysis must be in more than one direction, nevertheless renal rickets is so unusual that it must be regarded only as an exceptional cause of this condition.

As has been stated, the cause of slipping of the upper femoral epiphysis is insufficient strength in the newly formed layer of bone in the metaphysis next to the epiphyseal cartilage. This weakness naturally varies in degree, it may be so insignificant that great violence is required to cause displacement, or it may be so pronounced that the mere walking of the patient causes epiphyseal loosening. In one instance considerable displacement occurred while patient was lying in bed.

Up to the present I have spoken of the epiphysis becoming displaced; actually it remains in the acetabulum where it rotates backward and downward, while the femoral neck twists in the opposite direction, forward and backward. However, it is easier to describe and understand the movements of the epiphysis.

ANATOMY OF SLIPPING OF THE UPPER FEMORAL EPIPHYSIS

The head comprises that part of the upper end of the femur which is covered with a layer of articular cartilage about 2 millimeters thick. It is round and constitutes approximately three-quarters of a sphere. The neck extends from the outer edge of the head to the trochanteric area. In early childhood its entire surface is covered with cartilage, but after the age of 10 only its upper anterior portion (Fig. 1) is thus covered. The cartilage on the upper part continues directly into the cartilage in the greater trochanter.

The metaphysis (the zone of growth) is the part of the neck nearest to the epiphyseal cartilage and is comprised of three parts during the period now in question: (1) the zone of calcified cartilaginous cells adjacent to the epiphyseal cartilage, which are ready to become transformed into bony tissue; (2) newly formed bony tissue; and (3) a band of joint cartilage surrounding the metaphysis and comprising the lateral part of the joint surface of the head (Fig. 1, between *a–c*).

The head, i.e., the principal part of the upper end of the femur, thus includes the epiphysis and metaphysis. It is in the newly formed layer of bone of the metaphysis that displacement of the epiphysis takes place and not in the epiphyseal cartilage (Fig. 2). The surface of the epiphyseal cartilage facing the metaphysis is not smooth but unevenly furrowed and pitted, particularly near the periphery where it also curves down and covers the metaphysis. The articular cartilage totally follows the epiphysis when the latter displaces, taking with it the edges of the metaphysis (Fig. 2). These edges fill up the pocket formed between the distal free part of the joint cartilage and the periphery of the epiphyseal cartilage. The part of the epiphysis facing the metaphysis (the slipping surface) thereby becomes more rounded than if the slipping had taken place along the epiphyseal cartilage. The slipping epiphysis forms a rounded excavation against the metaphysis and the metaphysis a corresponding spherical surface. More easily to understand the slipping, it may be said that it occurs in a spherical articulation between the epiphysis and the metaphysis.

In pronounced displacement, as soon as the joint is opened, the upper anterior surface of the neck is found to be rounded at the point where previously it was concealed by the epiphysis. The epiphyseal cartilage is of course not a plain surface but is unevenly furrowed (Fig. 3). However, anteroposteriorly it is horizontal, although lateromedially there is an inclination of about 10 to 20 degrees. If epiphyseolysis appears, the epiphysis rotates backward and downward. In all probability it is the incessant movements taking place in the hip joint with the perpetually varying load on the head that break the already weakened connections between the epiphysis and metaphysis.

No special exertion is required to loosen the weak bond. As a rule, therefore, the first displacement or, perhaps, displacements are insignificant. It does not appear improbable that, at first, the slipping is continuous, or rather takes place by degrees. The more the epiphysis is shifted backward in this manner, the less support it receives posteriorly. The weight of the body, which previously appeared to be unevenly distributed with the pressure shifted somewhat backward, has an even greater action now that the epiphysis is beyond the metaphysis, and causes the epiphysis to rotate backward and downward toward the edge of the metaphysis. The farther back the epiphysis comes, the more it is exposed to body weight.

The foregoing may explain the fact that nearly all, or perhaps all cases of epiphyseal slipping, go through stages of minor displacements before a major one occurs, and that the later displacements are never as slight as the first ones.

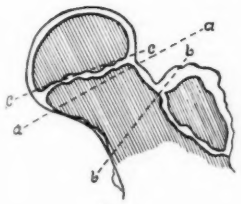


Fig. 1.

Fig. 2.

THE ROENTGENOGRAPHIC APPEARANCE OF EPIPHYSEAL SLIPPING

First let me say a few words about the x-ray examination. To be able to follow the development of epiphyseal slipping and, of even greater importance, in order to establish a diagnosis at the very beginning of the process, first class x-ray equipment is required and an operator who is not only a good technician but who is also specially trained to interpret what he sees.

As to the technique, the roentgenograms should always be taken at the same distance. The custom at the orthopedic clinic in Stockholm is to have 1 meter between the focus and the film. Similar exposures must be made of both hip joints on one and the same film. For example, if inward rotation is impossible in one hip, the other one must also be pictured in outward rotation, etc.

In epiphyseal slipping as in many other hip diseases, for example coxa plana, lateral views are the most informative. It must be considered a serious error, therefore, not to take a view in lateral position, Lauenstein's position, as a matter of routine in all hip diseases. The epiphysis displaces backward and downward, and obviously views in that position not only reveal to the best advantage the extent of the displacement, but are the first upon which it will appear. When taking these views, the patient's knee is supported with a hard, round, large cushion. The hips are abducted to 70 degrees and flexed to about 80 degrees with the same rotation on both sides; in the picture the greater trochanter should be seen projected onto the neck, the contours of the two bones coinciding as far as possible. In this way it is easy to check to see that both hips are in the same position. The picture is taken from the front with the legs parallel if possible and rotated, preferably to midposition. In the earlier stages the best way to discover the extent of the displacement is to cut the film in two and superimpose one picture on the other. Care should be taken to apply the outlines of the neck to each other, after which comparison of the peripheries of the two epiphyses reveals whether any slipping has taken place. Displacement in the

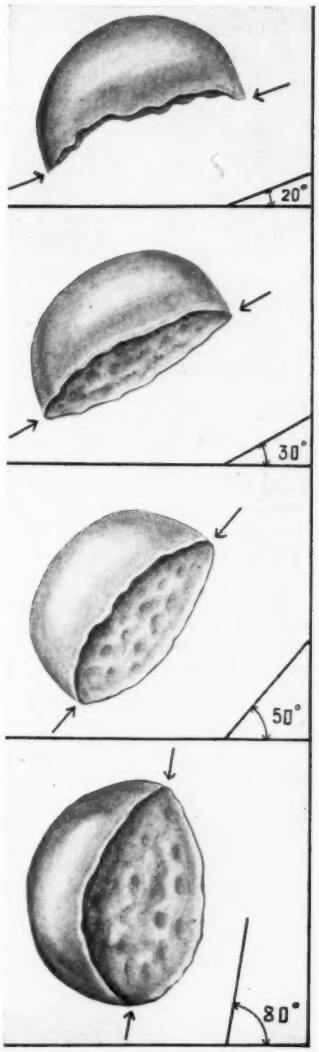


Fig. 3. Anteroposterior view of the epiphysis in three different stages of displacement. a, Normal position—20 degrees of inclination; b, early slipping—30 degrees of inclination and rotation backward on an axis indicated by the two arrows; c, more advanced slipping—50 degrees of inclination and rotation increased so that more is to be seen of the epiphyseal cartilage; d, maximal slipping—80 degrees of inclination and still more rotation.

postero-inferior part is shown best in the lateral view and displacement in the supero-external part in the anterior view. Good exposures in a suitable

a b c

Fig. 4. Case 1. a, July 2, 1936; b, October 24, 1936; c, November 27, 1937.

position will show slipping of the epiphysis in a very early stage when it is displaced less than 1 millimeter.

Epiphyseal slipping is always best diagnosed on the basis of a lateral view, i.e., in flexion abduction position, Lauenstein's position. A good example of this is the following case:

CASE 1. A boy of normal type, born 1920, during the spring of 1936 suffered periodically from pain in his left knee when walking. An x-ray examination of his hip was made at another hospital on July 2, 1936 (Fig. 4, a), from which I borrowed the film. I have included only the view in the lateral position. The epiphysis projects beyond the metaphysis like a small hook. Furthermore, the epiphyseal line is seen to be broader and more transparent than normal. The patient was treated, but for too short a time, and was readmitted to the hospital 3 months later with a more extensive displacement than on the first occasion (Fig. 4, b, October 24, 1936). He was then sent to my hospital, but during the trip his hip became more painful and the next picture, taken at my hospital, shows a maximal displacement. He was then put in skeletal traction with a weight of 8 kilograms for 10 days. Some improvement of the position of the epiphysis could be noted. He was then treated with continuous adhesive extension with a weight of 4 kilograms for 2 months, after which he stayed in bed with massage and gentle exercises for another month. He then walked with crutches for 6 months. In the roentgenogram the position of the epiphysis is seen to have improved but this is not entirely true, since during the year of treatment the body's reparative elements have been in action and the neck has been absorbed superiorly and built out inferiorly toward the epiphysis. The position of the epiphysis always looks better 12 months after it has fused with the metaphysis (Fig. 4, c).

CASE 2. A boy of normal type, born 1924, was knocked down in a football match on July 7, 1938. He had to lie down for a few hours after the accident, after which he could walk without pain. Ten days later he went to a hospital, where x-ray examination was said to reveal nothing abnormal, for which reason he received no treatment. Since he did not get better, he came to my hospital 5 months later. Roentgenograms taken then showed a distinct bony deposit on the lower part of the metaphysis which indicated a healed displacement. The supero-anterior part of the neck showed beginning absorption. The anterior view revealed clearly the low, medially displaced epiphysis. Nailing was then done with a Smith-Petersen nail.

I have since been able to borrow the roentgenograms taken at the first hospital. A comparison of the pictures of the two hips in lateral view reveals the displacement. The "epiphyseal hook" downward and medial displacement of the epiphysis can be seen. The anterior view, on the other hand, appears normal, except that the epiphyseal line is somewhat broader than in the sound side (Fig. 5, a and b).

Thus, in early cases, it is sometimes impossible to see the displacement of the epiphysis in an anterior view. However, on this picture a condition is seen which is occasionally inaccurately described as the preslipping stage. If the slipping is a little more pronounced than in this case it will be seen from the next case that early stages of epiphyseal slipping can be diagnosed from an anterior view; but this does not alter the fact that a lateral view must also always be taken.

CASE 3. A boy born in 1925 had been limping slightly for a month. He was subjected to x-ray examination at another hospital where the verdict was: normal hips and no treatment. He gradually became worse until, finally, one day after gymnastics 4 months later he could not walk. The following day he was roentgenographed and on this occasion the anterior view revealed distinct slipping (Fig. 6, September 16, 1937). Films from the first examination were borrowed and showed the epiphysis to be lowered 1 millimeter and medially displaced 2 millimeters (Fig. 6, May 18, 1937). The comparison is best made by placing the pictures of the two hips on each other (see the contour of both epiphyses superimposed). The epiphyseal line is broader and more uneven than normal. This might also have been called the preslipping stage, but, as we see, it is a minimal displacement recognizable even though no lateral view was taken.

CASE 4. A boy born in 1925, of the adiposogenital type, had limped slightly for a month. He went to a hospital where his hips were roentgenographed and pronounced normal. He became worse and therefore came to my hospital 7 months later. The first x-ray film shows a distinct minimal slipping. The displaced part of the epiphysis looks like a small hook (Fig. 7, a).

As usual, the epiphyseal line is broader, due to the fact that the newly formed bony tissue in the metaphysis i-

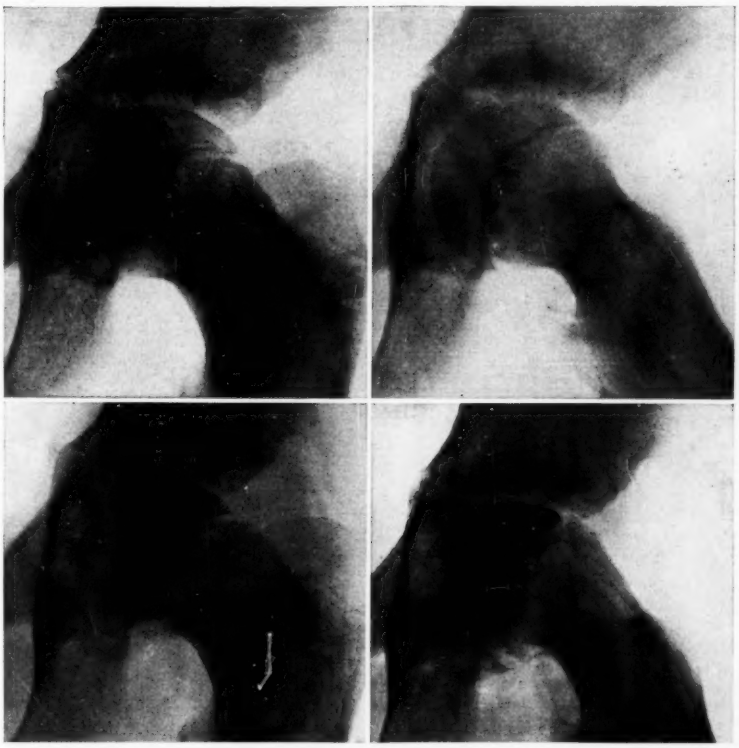


Fig. 5. Case 2. a, Above, July 12, 1938; b, below, November 8, 1938.

chipped. Small splinters naturally get out of place and thus cause the uneven appearance of the surfaces facing one another. The anterior view also reveals the widened epiphyseal line and a medial displacement of the epiphysis. Roentgenograms (Fig. 7,b) taken May 28, 1938, 7 months after the first ones, show that a bracket has been built out after an earlier displacement, but that the epiphysis lacks support to some extent, indicating a rather recent displacement.

CHOICE OF TECHNIQUE

As to the choice of method I shall repeat what I have said before. Reduction under anesthesia should never be done, and this for two reasons: It generally does not result in reposition and, what is more important, the function of the joint is completely destroyed in one-fifth of the joints treated in this manner. After the so called reduction, which takes place with the hip greatly rotated inward, and after the plaster is applied in the same position, both hips are roentgenographed. In order to demonstrate the difficulty of judging the relationship of the epiphysis to the metaphysis in the different stages of rotation, I have produced an epiphyseal slipping in a preparation from an 11 year old child (Fig. 8). The upper pictures show the epiphysis fixed and roentgenographed as usual in the anteroposterior and lateral views (Fig. 8, a and b). Movements were then made with continued fixation in the same position between the epiphysis and metaphysis. The hip was then roentgenographed in internal rotation of 40 degrees, i.e., as much as could be done normally. The roentgenogram shows the lower outline of the epiphysis to coincide with that of the metaphysis (Fig. 8, c). It resembles very closely an x-ray picture showing a successful reduction. The next picture shows internal rotation of 50 degrees and abduction of 40 degrees (Fig. 8, d). Here it appears as if the displacement had been overcorrected. Compare with the pictures of a case of reduction which I recently borrowed from another hospital. Figure 9, a, shows fresh slipping; b, after 10 days of skeletal traction; c, the same position between

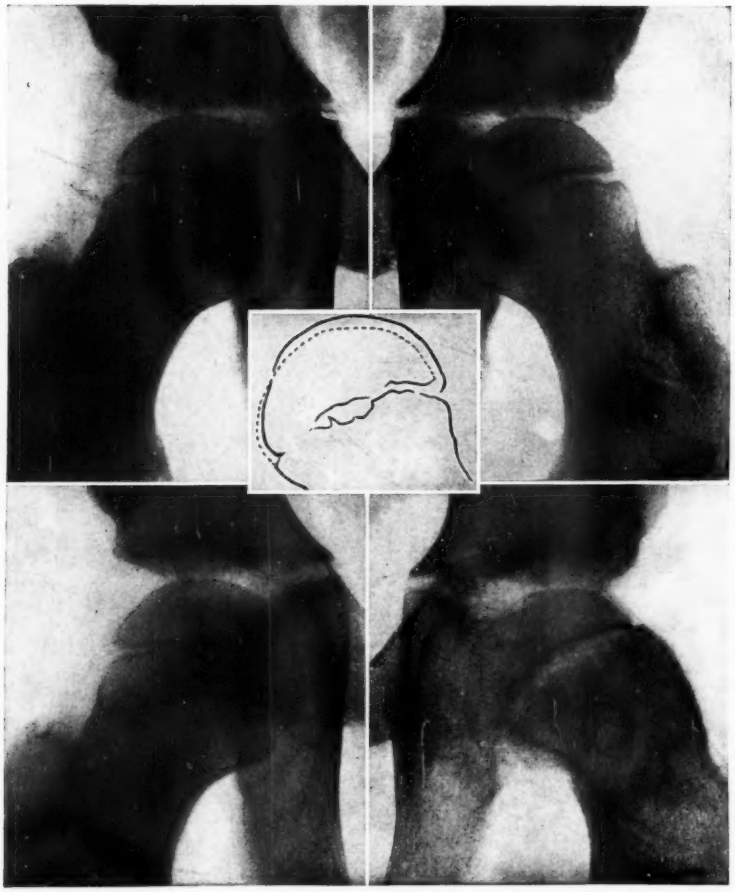


Fig. 6. Case 3. a, Above, May 18, 1937; b, below, September 16, 1937.

epiphysis and metaphysis as in b, but there is inward rotation 40 degrees.

It is impossible to determine the position of the epiphysis unless symmetrical pictures of both hips are available for comparison. A careful examination of the so called successful reductions will reveal that very few of them show any improvement whatever; in other words the results are extremely poor.

A review of my cases previous to 1924 when I stopped performing reduction under anesthesia shows that, in 4 of 25 cases, the head of the femur became partially necrotic. In short, the treatment caused actual damage in one-fifth of the cases in my series (Fig. 10).

McMurray said in 1938: "In 25 per cent of cases treated in this manner rigidity of the joint appears at a later date after an apparently satisfactory increase of movements. Such rigidity is caused by the development of arthritic changes which are the result of widespread soft tissue injury and interfere with blood supply."

Philip Wilson has followed 16 of his cases treated with closed reduction and found "a high incidence of stiffness and restricted motion." He attributes these poor results to the treatment, which he discarded in 1922 upon discovering its unsuitability.

I have never observed necrosis of the head in cases given the adhesive extension treatment, which I have used since 1924. In my cases, opera-

Fig. 7. Case 4. a, Above, November 5, 1937; b, below, May 28, 1938.

tive reduction without any damage to the ligamentum teres has given excellent results as far as the position of the epiphysis is concerned but, like the "closed reduction," entailed the risk of the head necrosing. Therefore, this method also cannot be recommended. The foregoing should emphasize my idea of how epiphyseal slipping should not be treated.

As to how recent epiphyseal slipping should be treated, I have found the following to be satisfactory.

Until last summer, all my cases were treated with adhesive extension, with the hip first in midposition and then in gradually increased abduction and internal rotation. A weight of 4 to 5 kilograms was used for the purpose. After 2 months the bandages were removed, but the patient remained in bed for another month and was given massage and gentle exercise. Crutches were then used for 6 months and afterward two sticks until the x-ray revealed that the epiphyseal line had closed, which took about 1 year. I have used this method more than any other, and consider it to be the most conservative and to give as good results as reduction under anesthesia but without any risk for necrosis. However, it involves some risk of recurrence with consequent poor results.

While in America in the winter of 1938, I learned a new method which obviates this risk and is perhaps better in other respects. I was fortunate in being able to see Philip Wilson at work in New York. Like many other surgeons, he used to attempt to perform reduction under narcosis, but he abandoned this method as long ago as 1922, since he found that it seldom if ever was successful and, in several instances, was followed by necrosis of the femoral head. Since 1934 he has used nail fixation in the treatment of slight displacement,

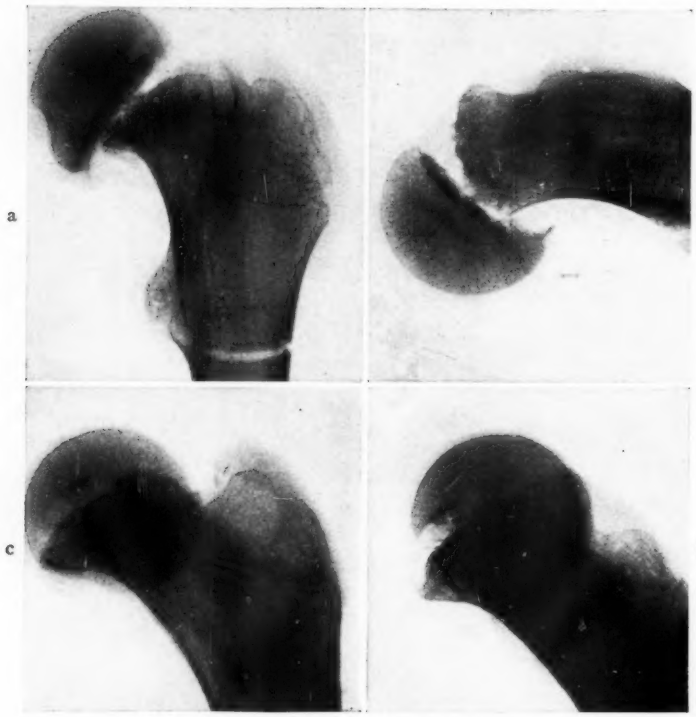
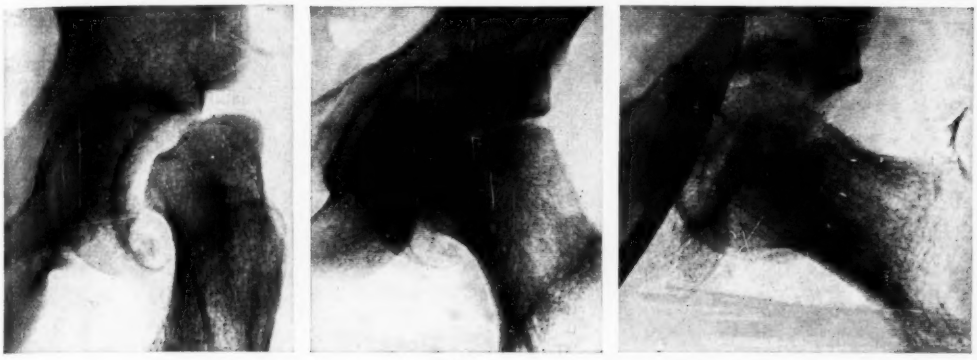


Fig. 8, a, b, Epiphysis fixed and roentgenographed in anteroposterior and lateral views; c, epiphysis coincides with metaphysis; d, internal rotation of 50 degrees and reduction of 40 degrees.

i.e., in cases in which the lateral roentgenogram shows that "the epiphysis has not displaced posteriorly more than one-third of the diameter of the neck." He uses the Smith-Petersen nail for the purpose. I had an opportunity to see several of Wilson's cases, of which there are 9, the first one having been operated upon in 1934. I found the results to be good. A few months after my return to Sweden, one of my patients, who had a minimal slipping on one side, which had been stationary for 1½ years and therefore was considered healed, had a new displacement. Displacement was so great that it was impossible to treat it either with adhesive or nail extension. If nailing had been done in time in this case, the patient would in all probability now have a normal hip. In order to avoid such disasters, I decided to nail all cases of epiphyseolysis, according to the method of Wilson. Since then 5 patients have received this treatment. As prescribed by Wilson, they have been kept in bed for a month and then have used crutches for another month, after which they have gone back to school, but have taken no part in any sport until the epiphyseal line has closed, which Wilson states usually takes place within a year, at which time he removes the nail.

The follow-up period has been too short to provide any conclusive evidence in the 5 patients treated by nailing at my hospital since the summer of 1938, but I intend to continue using Wilson's method for the present.[1] With regard to the technique, the direction of the nail must be adjusted to correspond with the position of the head, i.e., more backward and less upward than in reduction of a fracture of the neck. The position of the head is about the same as that found in an unreduced fracture of the neck. The drill is inserted by hand and directed against a scale in the groin. In my opinion, it is not so important to go so deep into the head as in fractures of the neck, and probably

[1]A re-examination of my nailed cases was made in 1940, however, and all of them had gone back to school walking without limping and showing nearly normal mobility of their hips.



a b c

Fig. 9. Roentgenograms from case in another hospital. a, Fresh slipping; b, after 10 days; c, same as in b but inward rotation of 40 degrees.

all that is required is to nail right through the epiphyseal cartilage. The healing conditions also are much more favorable than in a medial fracture of the neck.

Therefore, it is possible that this treatment is definitely indicated for minor epiphyseal slipping. However, for more advanced slipping it is not so simple to decide what is best, except when it is a question of severe displacement or cases in which the epiphysis has fused. Then cuneiform torsion osteotomy should be performed.

There comes a day for all these cases of epiphyseolysis when the internal secretions are balanced and no further displacement can occur. The femoral head then fuses wherever it happens to be. Reparatory processes are initiated. Superfluous bony parts are absorbed and gaps are filled in accordance with the usual laws of regeneration in the skeletal system. The part of the neck projecting upward and forward, where the head was once attached, is absorbed. This remodeling process is illustrated in 3 pictures (Fig. 11), which show the rapid development of this remodeling process during 1 year. The mobility of the hip increases as the absorption proceeds.

The development of an epiphyseal displacement into coxa vara may be followed in some pictures. Lateral views of these early cases show bony tissue growing out inferoposteriorly from the neck to meet the slipped epiphysis. They also reveal that the projecting part of the neck, where the epiphysis previously had its place, is beginning to be absorbed. The later development can be studied in Figure 12, which shows how the inferoposterior part of the neck grows out and entirely fills up the space between the epiphysis

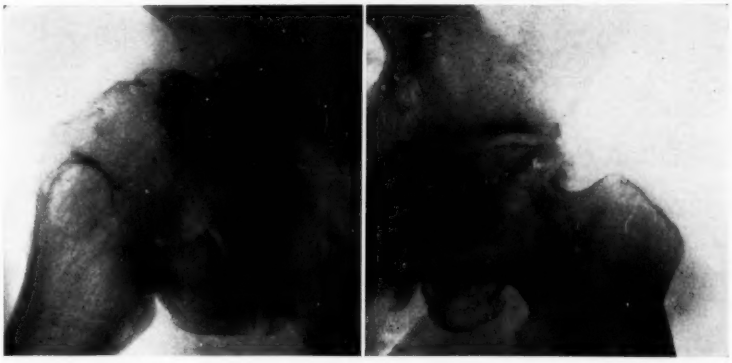


Fig. 10. Right hip ankylosed mobility of left greatly limited.

Fig. 11. Remodeling process: top, August 18, 1937; middle, November 3, 1937; and, below, May 28, 1938.

and neck, while, at the same time, the upper projecting part of the neck, where the epiphysis used to be attached, is absorbed. The upper outline of the neck thereby becomes convex and the lower outline concave, giving the impression that the entire neck is curved. The spongy framework in the neck also begins to adapt itself to the new static conditions; Figure 13 illustrates a later stage in the evolution into coxa vara. The curved form of the neck and its spongy framework is even more distinct as well as the enormously increased density of the compact tissue in the lower part of

Fig. 12. Inferoposterior part of neck is grown out and fills space between epiphysis and neck.

the neck, where the weight of the body is concentrated and the need for strength most pronounced.

The slipping may stop at any point. Therefore the epiphysis may become fused after such an insignificant displacement so that it can scarcely be detected that it ever had slipped. I believe that it is of great importance not only to discover epiphyseolysis as early as possible, but also to have the epiphysis fused in its new position as rapidly and with as little traumatism as possible. We know that in cases of solution of continuity of any part of the skeleton, the more completely immobilization is carried out the less callus is formed during the healing process. I think we are dealing with the same problems which led Hugh Owen Thomas to lay special stress on the importance of rest. The same is true with regard to fusion of the epiphysis after slipping. If the patient is allowed up too soon, there is a risk not only of further displacement, but also of more callus being formed around the border of the slipped epiphysis; marginal osteophytes arise with the consequent danger of an early appearance of arthritis deformans.

A number of early cases of arthritis deformans in the hip joint are undoubtedly caused by incompletely healed epiphyseolysis during childhood in which the patient never stayed in bed, so that the healing was constantly disturbed but only very slight slipping was caused. An insignificant displacement may present so few symptoms during childhood that it is forgotten by the time the patient is grown up. Many cases of arthritis deformans in adults have their origin in a congenital deformity or in a deformity which had been acquired during childhood. It is very often difficult to determine to what morbid process during childhood or adolescence secondary arthritic changes are due, unless the cases have been followed from the beginning.

As we know, the articular cartilage is nourished by the synovia. Normal mobility is, therefore, of great importance in the transportation of the nutritive fluid, and a normal capsule is essential for the production of the necessary amount of joint fluid and for its proper composition. If the nutrition of the head is disturbed due to more or less extensive tears and if the epiphysis heals with edges, the capsule also suffers injury and its capacity to nourish the cartilage is thereby reduced. The nutrition of the articular cartilage is then not the same as in a normal joint, and such a condition favors the early appearance of arthritis deformans. The most severe cases of early arthritis deformans which I have seen are those which have undergone so called reduction under narcosis and developed more or less extensive partial necrosis of the head. I myself performed reposition in a case of epiphyseolysis—in one hip in 1913 and in the other in 1914. Roentgenograms taken immediately after the operation show what is popularly supposed to be successful reduction on both sides; that this was not the case is now obvious, and that the patient suffers great discomfort from the ensuing arthritis deformans is clear from the picture.

The series of roentgenograms presented were selected from my material to illustrate certain important points.

Fig. 13. Later stage in evolution of coxa vara.

Some improvement in position may be obtained by means of adhesive extension or a short period of wire extension (10 days at the most) with the hip in outward rotation.

The so called reposition under narcosis is, as a rule, no reposition at all; it is a misinterpretation of the roentgenograms.

Reposition under narcosis should never be performed, since, in about every fifth case, it entails destruction of the joint (necrosis of the head).

Reposition by means of arthrotomy may give excellent results, but this method also is inadvisable, since it is attended with the same risk (necrosis of the head), even if the ligamentum teres has been spared.

Reconstructive processes following epiphyseal displacement often proceed rapidly and thus cause an apparent reposition.

Epiphyseolysis may develop into coxa vara.

Premature arthritis deformans may appear in patients who have had epiphyseolysis in their youth particularly if they have undergone reposition under narcosis.

It is my belief that premature arthritis deformans can be prevented if diagnosis is made early and conservative treatment carried out efficiently and for a long period, in order to allow the even contours of the head to return.

CONCLUSIONS

The diagnosis of slipping of the femoral head while the slipping is still minimal is of extreme importance in the prognosis. The symptoms must never be made light of. A youngster who limps, or whose parents state that he occasionally limps, should be subjected to a thorough examination. Even if examination reveals that there is present only the slightest limitation of mobility, a roentgen-ray examination should immediately be performed and the roentgenograms should be carefully studied.

In the early stages the diagnosis should not be made from an anteroposterior view, the only significant signs are revealed in the lateral view. The significant signs are three, namely: the epiphyseal hook, down; the metaphyseal edge, up; and the broader epiphyseal line.

Entirely satisfactory therapeutic results can be obtained only if the diagnosis is made at an early stage. As soon as the condition is diagnosed, the patient should be hospitalized, since another and perhaps more serious displacement may occur at any time. The treatment should be continued until the epiphysis has become so well fused that further slipping is impossible. The best method when conditions are not too severe is the one in which a Smith-Petersen nail is applied after the method of Wilson and this method can be used as long as two-thirds of the epiphysis is in contact with the metaphysis.

The sound hip should be carefully supervised during the whole course of the treatment, since in 25 per cent of the cases the condition becomes bilateral.

THE TREATMENT OF ADYNAMIC ILEUS BY GASTRO-INTESTINAL INTUBATION IN CHILDREN

GROVER C. PENBERTHY, M.D., F.A.C.S., R. J. NOER, M.D., F.A.C.S., and CLIFFORD D. BENSON, M.D., F.A.C.S., Detroit, Michigan

ADYNAMIC ileus, always a dreaded surgical complication, is apt to be particularly dangerous in children. The lability of children in illness is familiar to all; their reaction to distention is particularly marked. They show the effects of starvation very early in a tendency toward acidosis, with more rapid wasting, dehydration, and mineral loss. These factors coupled with the added difficulties in treatment justify a special consideration of the problem of distention in children. The causes of ileus are much the same as in adults and may be classified as follows: (1) Postoperative, presumably on basis of trauma; (2) intraperitoneal inflammation—peritonitis, abscess, etc.; (3) extraperitoneal inflammation, trauma, toxemia—retroperitoneal, hematoma, fractures of spine and pelvis, renal lesions, pneumonia, etc.

Experimental evidence indicates that adynamic ileus is produced by the agents named through a reflex inhibition of the normal intestinal motility (2, 12, 15). A physiological ileus follows laparotomy (12, 18) and it is only when it fails to subside that it can properly be termed paralytic, or adynamic ileus. The sequence of events is no different in children; while mild degrees are less common than in adults, severe adynamic ileus is less well tolerated due to the factors mentioned.

Various forms of treatment have been proposed and their very multiplicity is eloquent testimony to the fact that no one of them has proved uniformly satisfactory. Most important is undoubtedly prophylaxis; adequate pre-operative preparation both physical and psychic, with adequate fluid intake and avoidance of catharsis will do much to minimize postoperative distention. Likewise gentleness of all operative procedures, attention to the problem of water balance (3), and avoidance of excessive stimulation of gastro-intestinal tract by catharsis and enemas during the postoperative period will further aid in keeping down the incidence of ileus.

From the Department of Surgery, Wayne University College of Medicine, the Children's Hospital of Michigan, and the Detroit Receiving Hospital.

Aided by a grant from the Committee on Scientific Research of the American Medical Association.

Read before the Western Surgical Association, Los Angeles, California, December 15, 1939.

Once adynamic ileus has appeared we are faced with the need (particularly urgent in children) for some means of reducing the distention with a minimum of disturbance to the patient. Methods which have been proposed for the treatment of ileus may be listed as follows: (1) enemas and local applications, (2) drugs, (3) oxygen therapy, (4) spinal anesthesia, (5) enterostomy, (6) suction drainage—(a) gastric, (b) duodenal, (c) intestinal.

Enemas, stupes, and other local applications have been used for many years in the treatment of all forms of distention. Enemas at best empty only the colon with little or no effect upon the distention of the small intestine; they are somewhat irritating to the colon and upsetting to the patient. It has been pointed out by Ochsner (19) that they frequently actually aggravate the condition they are meant to relieve. Stupes and other local applications probably have no effect upon the distention and their repeated application adds another factor to disturb the patient's rest. There is some evidence that external dry heat to the abdomen in the form of a light cradle may be both soothing to the patient and helpful in reducing the effects of distention (16).

Drugs, among them pituitrin, eserine, pitressin, prostigmine and intravenous salt solutions, have seen considerable use. Many of them are ineffective even when tested experimentally; all have the disadvantage that their effectiveness is dependent upon stimulation of musculature which is already overloaded by distention. The activity of these various drugs has been well summarized by

TABLE I.—ADYNAMIC ILEUS IN CHILDREN

Initiating lesion	Cases	Lived	Died
Appendicitis—			
Acute	4	4	
Abscess	8	8	
Local peritonitis	6	6	
Diffuse peritonitis	10	8	2
Gunshot—abdomen	2	2	
Tuberculous peritonitis	2	1	1
Atony with partial obstruction	1	1	
	33	30	3
Per cent	....	90.9	9.1

TABLE II.—ADYNAMIC ILEUS COMPLICATING APPENDICITIS IN CHILDREN

Type	Cases	Distention			Decompressed		Result	
		Mild	Moderate	Severe	Stomach or duodenum	Intestine	Lived	Died
Acute	72	1	2	1	3	1	72	0
Recurrent	39	0	0	0	0	0	39	0
Abscess	21	3	3	2	7	1	21	0
Perforated with local peritonitis	26	4	2	1	5	1	26	0
Perforated with diffuse peritonitis	14	1	6	4	6	4	12	2
	172	9	13	8	21	7	170	2

Ochsner, Gage, and Cutting (20), and will not be discussed further. These authors have also studied the action of hypertonic salt solutions (21) as suggested by Hughson and Scarff. These solutions, probably the most effective of this group of agents, are limited by the muscular overload already discussed and by the fact that they are not without some disadvantages in the matters of toxicity and the possibility of local vascular damage. At times they are helpful adjuncts to other forms of treatment.

Recently Fine and his co-workers have reported good results from the use of 95 per cent oxygen in the treatment of distention. Requiring special apparatus at first, the advent of the Lovelace-Boothby (11) mask has simplified the procedure. The effectiveness of this agent has been encouraging and it is certainly deserving of a more extended trial.

Spinal anesthesia has undoubtedly been helpful in many cases of adynamic ileus in adults (4, 6, 13, 24, 25). It is frequently ineffective, however, and in such cases represents an heroic measure resorted to without avail (23). In young children it is not without great danger of a lethal outcome, and it would seem preferable to resort to simpler and more uniformly effective methods when such are at hand.

The place of gastric and duodenal suction drainage in adults is now well established, and the work of Ward and of Wangensteen (28) in this regard is familiar to all. Wangensteen has emphasized the greater effectiveness of a tube lying beyond the pylorus as compared to drainage from the stomach alone. Since a considerable part of the distending gas is due to swallowed air (14, 26) this type of suction is particularly effective prophylaxis against the development of ileus in the type of case prone to develop this complication. A large proportion of the cases with adynamic ileus can also be decompressed by this type of drainage alone (22). However, there have always remained some cases in which an intractable ileus failed to yield to suction from the stomach or duodenum.

After considerable experience with intestinal intubation in adults (1, 8, 9, 10, 17, 22) we found ourselves called upon to attempt the method in children. At first thought it seemed that these

TABLE III.—INCIDENCE OF DISTENTION ACCORDING TO TYPE OF APPENDICEAL PATHOLOGY

	Cases	Distention		Suction drainage	
		No.	Per cent	No.	Per cent
Acute	72	4	5.5	4	5.5
Recurrent	39	0	0	0	0
Abscess	21	8	38.0	8	38.0
Local peritonitis	26	7	27.0	6	23.0
Diffuse peritonitis	14	11	78.6	10	78.5

TABLE IV.—RELIEF OF DISTENTION IN CHILDREN

	Number	Per cent
Cases decompressed	33	
Suction from stomach or duodenum	22	66.7
Suction from intestine	11	33.3

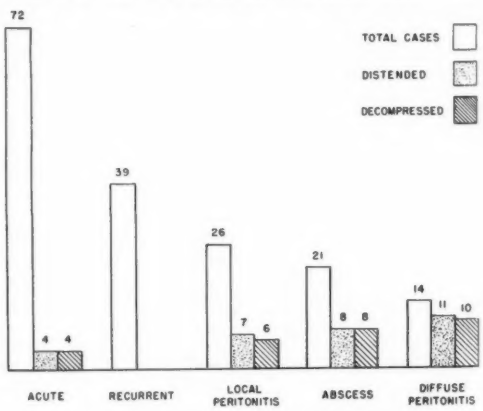


Fig. 1. Appendicitis and distention.

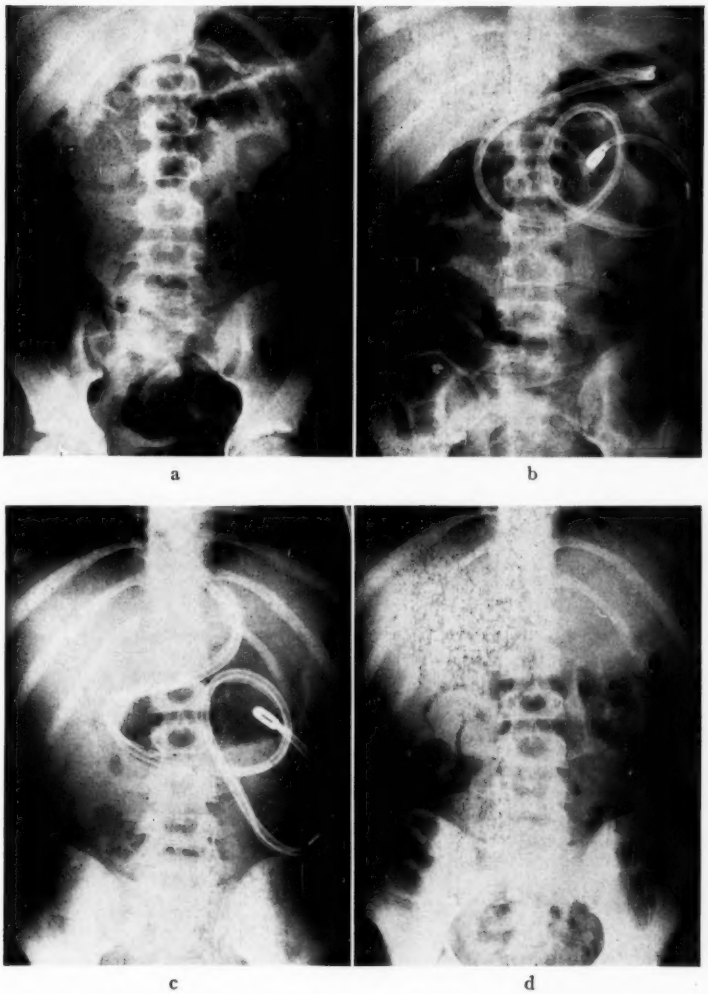


Fig. 2. a, November 18, 1939; b, November 20, 1939; c, November 27, 1939; d, December 1, 1939.

young patients would be difficult to handle by this method, but experience has proved otherwise. By and large we have found the children more co-operative than adults, and when approached with sympathetic understanding they respond with admirable co-operation. Their smaller nostrils have prevented us from using the tube which we prefer, necessitating use of the double lumen tubing which we find generally less efficient, but which has proved adequate in the cases reported. Even more careful attention to the details of the constant operation of suction and to replacement of the withdrawn fluids and salts is essential in the treatment of children.

Wangensteen has rather aptly pointed out in discussing the shortcomings of suction drainage that, "In the interval during which one waits for the obstructing mechanism to relent, the gut above the obstruction cannot be employed as a nutritive tube, as it can when the gut is drained

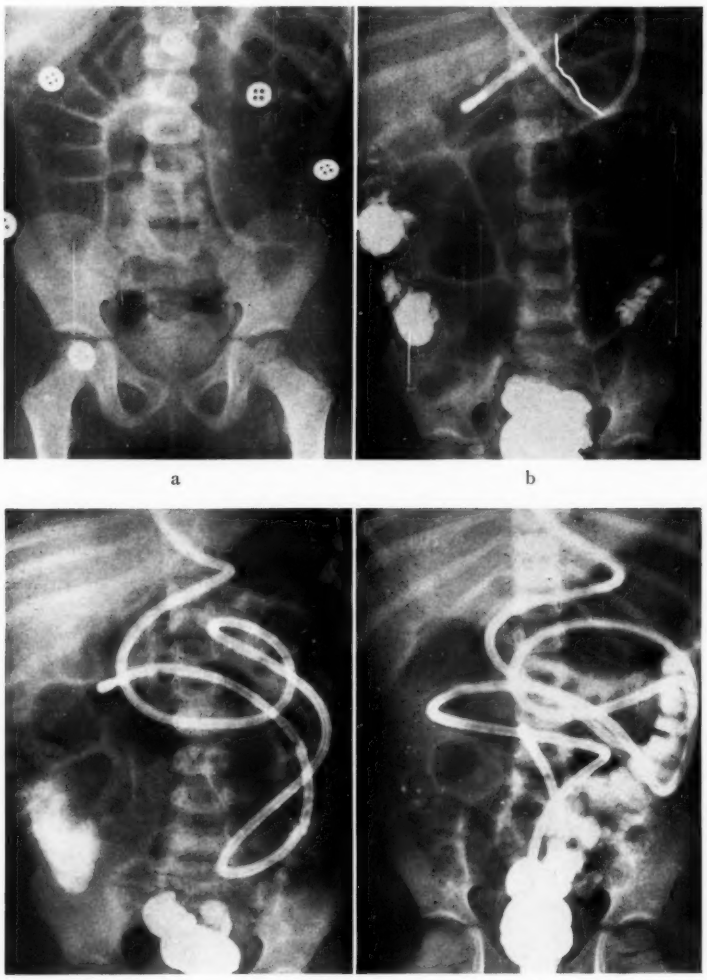


Fig. 3. a, October 22, 1938. Barium enema was given before consultation on October 22 because of a suspected lesion of the large bowel; b, October 24, 1938; c, October 26, 1938; d, October 27, 1938.

near the point of obstruction" (27). This fact is particularly important in children, who quickly show the ill effects of the loss of essential fluid and salts. With the tube passed into the lower reaches of the small bowel this disadvantage is overcome, for most of the absorptive area lies above the point from which suction is exerted; nutrition can thus be maintained by oral feeding alone (17). This advantage is also present in the cases in which enterostomy has been performed for acute intestinal obstruction.

During the past year 33 cases of distention in children have been treated by means of gastro-intestinal intubation at the Children's Hospital of Michigan and the Detroit Receiving Hospital (Table I). As might be expected, the majority of these resulted from appendicitis, probably the most frequent cause of severe ileus in children.

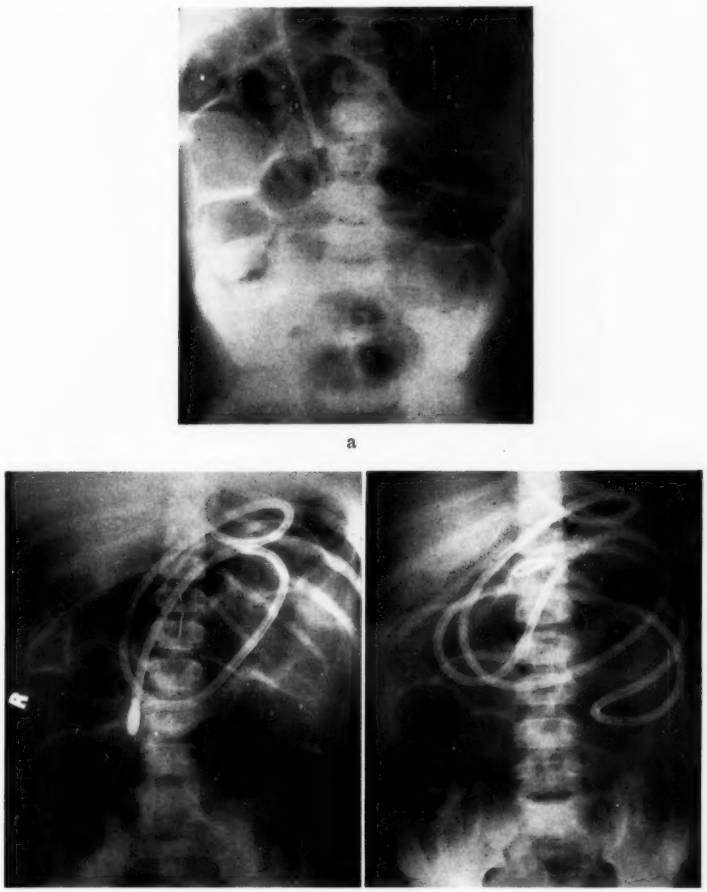


Fig. 4. a, July 3, 1939; b, July 8, 1939; c, July 10, 1939.

While this is not intended as a presentation of cases of appendicitis, it is worth while to point out several important facts emphasized by the data. That the mortality from appendicitis in children need not be excessive is apparent from a study of the 172 such cases here presented (Table II). While the mortality in this group was quite low (1.1 per cent) we do not feel that the series is large enough to indicate a mortality figure which might routinely be expected in the handling of all types of appendicitis. Nevertheless it does indicate that in early appendicitis with proper handling the mortality can be kept at a minimum. An additional point which might be emphasized is that in this group the incidence of ileus was low. None of these patients were operated upon through a right rectus muscle splitting type of incision; the adoption of an incision which approaches the appendix from directly over the cecum has undoubtedly contributed to the low incidence of postoperative distention. In those cases in which ileus did occur early use of the tube tended to reduce its severity and duration. In this regard it is likewise interesting to note the direct relationship between the severity of the disease and the incidence of ileus; (Fig. 1 and Table III) none of the recurrent cases and only an occasional case of simple acute appendicitis showed postoperative distention, while this complication was almost the rule in the various forms of appendiceal

peritonitis. The series treated by intubation also includes 5 cases of distention from other causes (Table I).

All but one of these cases were successfully decompressed: in 1 case of tuberculous peritonitis the distention was only partially controlled, but sufficiently so to prevent its being a determining factor in the eventual outcome. It is worthy of note that a balloon tipped tube lying in either stomach or duodenum will provide drainage from these areas equal in efficiency to Levin or Wangensteen tubes; and it has the added advantage that it can be passed further down the intestine when gastroduodenal drainage is inadequate. In this series gastric and/or duodenal suction was effective in 22 cases (66.7 per cent) while in 11 (33.3 per cent) relief was obtained only when the tube tip had been passed into or beyond the jejunum (Table IV).

The following cases illustrate the use of intestinal intubation in the treatment of ileus in children:

C. P. A 12 year old boy suffered a gunshot wound of the abdomen, with through-and-through perforation of the stomach. Immediate suture was carried out and the boy developed a moderately severe degree of abdominal distention after operation, despite gastric suction instituted immediately after operation. He was successfully decompressed by means of a tube passed into the small intestine which remained in place for 16 days. An associated fracture of the body of the second lumbar vertebra may have been contributory to the development of the ileus.

E. D. (Fig. 2). A 12 year old boy developed generalized abdominal pain associated with nausea and vomiting, 3 days before admission. The pain localized to the right lower quadrant. Following an enema and a cathartic his pain decreased for a few hours the day before admission, then increased with more severity. When he entered the hospital the entire abdomen was tender and tense, and the boy appeared very ill. His distention was moderately severe and a diagnosis was made of diffuse peritonitis with associated adynamic ileus. He was treated conservatively, his distention controlled by intestinal intubation. The boy made a good recovery and left the hospital to return later for an interval appendectomy. Undoubtedly the control of his distention was a material factor in the favorable outcome of his peritonitis.

B. A. B. (Fig. 3). A 3 year old white girl developed peri-umbilical pain, nausea, and vomiting the day before admission to the hospital. She was admitted with a temperature of 102 degrees with marked abdominal distention, generalized pain, and rigidity. A diagnosis of diffuse peritonitis with associated adynamic ileus was made, and conservative treatment was decided upon. She was successfully decompressed by means of intestinal intubation and her peritonitis subsided. She was discharged from the hospital in good condition to return later for an interval appendectomy. Undoubtedly the control of her distention was a definite factor in her recovery from the peritonitis.

K. M. (Fig. 4). An 8 year old white boy suffered generalized abdominal pain with nausea and vomiting 3 days before admission. His pain localized in the right lower quadrant during the day preceding admission and there was associated diarrhea for 12 hours. Abdominal examination revealed generalized tenderness and rigidity, most marked in the right lower quadrant. Temperature was 100.4 degrees, pulse 120. Leucocyte count 14,300; 96 per cent polymorphonuclear cells. A diagnosis of acute appendicitis with perforation and early peritonitis was made.

Immediate operation was carried out and a ruptured gangrenous appendix was removed. His postoperative course was reasonably good until the second postoperative day when abdominal distention became quite marked. This was controlled by gastroduodenal suction, but the distention recurred on the eleventh postoperative day. Three days of gastroduodenal suction was ineffective in controlling the distention, and a balloon-tipped tube was passed on the fifteenth postoperative day. The patient's condition was markedly improved the following day with the tip of the tube lying in the intestine. Complete decompression was rapidly accomplished and the balloon-tipped tube was removed 5 days after its insertion. Patient's recovery thereafter was uneventful.

SUMMARY

1. Adynamic ileus is a serious condition in children, who stand distention less well than adults. A brief summary of methods for combating distention is given.

2. Evidence is presented for the viewpoint that gastro-intestinal suction drainage is the most logical and effective of these methods.

3. Intestinal intubation is practical in children and is often more easily accomplished than in adults. Having all the advantages of gastric or duodenal tubes it is frequently effective when these methods fail.

4. Appendicitis and its complications are the most common causes of severe ileus in children. The incidence of distention is directly proportional to the extent of the disease.

5. Thirty-three children with marked distention have been decompressed, 22 by suction from the stomach or duodenum and 11 by small intestine intubation. In many of these cases control of the distention has been the factor determining the successful outcome.

BIBLIOGRAPHY

1. Abbott, W. O., and Johnston, C. G. Intubation studies of the human small intestine; X. A non-surgical method of treating, localizing and diagnosing the nature of obstructive lesions. Surg., Gynec. & Obst., 1938, 66: 691–697.
2. Bayliss, W. M., and Starling, E. H. The movements and innervation of the small intestine. J. Physiol., 1899, 24: 99–143.
3. Coller, Frederick, A., and Maddock, Walter G. Dehydration attendant on surgical operations. J. Am. M. Ass., 1932, 99: 875–880.
4. Duval, M. Pierre. Spinal anesthesia in the treatment of acute intestinal obstruction. Bull. et mém. Soc. nat. de Chir., 1927, 53: 169–177.
5. Fine, J., Banks, B. M., and Hermanson, L. The treatment of gaseous distention of the intestine by the inhalation of ninety-five per cent oxygen. Ann. Surg., 1936, 103: 375–387.

6. GREIG, D. M. Spinal anesthesia in post-operative and other forms of ileus. Edinburgh M. J., 1927, 35: 470–475.
7. HUGHSON, WALTER, and SCARFF, J. E. The influence of intravenous sodium chloride on intestinal absorption and peristalsis. Bull. Johns Hopkins Hosp., 1924, 35: 197–201.
8. JOHNSTON, C. G. Decompression of the small bowel in intestinal tube drainage at site of obstruction. J. Michigan State M. Soc., 1938, 37: 623.
9. JOHNSTON, C. G., PENBERTHY, G. C., NOER, R. J., and KENNING, J. C. Decompression of the small intestine in the treatment of intestinal obstruction. J. Am. M. Ass., 1938, 111: 1365–1367.
10. LOFSTROM, J. E., and NOER, R. J. Use of intestinal intubation in localization of lesions of gastrointestinal tract. Am. J. Roentgenol., 1939, 42: 321.
11. LOVELACE, W. R. Technique of treatment of helium and oxygen using B. L. B. inhalation apparatus. Proc. Staff Meet. Mayo Clin., 1938, 13: 790–791.
12. MARKOWITZ, J., and CAMPBELL, W. R. The relief of experimental ileus by spinal anesthesia. Am. J. Physiol., 1927, 81: 101–106.
13. MAYER, A. Zentralbl. f. Chir., 1922, 49: 1882–1885.
14. MCIVER, M. A., BENEDICT, E. B., and CLINE, J. W. Postoperative gaseous distention of the intestine. Arch. Surg., 1926, 13: 588–604.
15. MELTZER, S. J., and AUER, JOHN. Peristaltic movements of the rabbit's cecum and their inhibition. Proc. Soc. Exper. Biol. & Med., 1906, 4: 37–40.
16. MULLER, E. F. Ueber den paralytischen Ileus. Mitt. a. d. Grenzgeb. d. Med. u. Chir., 1929, 41: 17–42.
17. NOER, R. J., and JOHNSTON, C. G. Decompression of the small bowel in intestinal obstruction. Am. J. Digest. Dis., 1939, 6: 46.
18. OCHSNER, ALTON. Postoperative treatment based on physiologic principles. South. Surgeon, 1935, 4: 197–206.
19. Idem. Postoperative treatment. South. M. J., 1936, 29: 53–57.
20. OCHSNER, ALTON, GAGE, I. M., and CUTTING, R. A. The value of drugs in the relief of ileus. Arch. Surg., 1930, 21: 924–958.
21. Idem. Influence of hypertonic salt solutions on the motility of normal and obstructed intestine. Arch. Surg., 1933, 27: 742–770.
22. PENBERTHY, G. C., JOHNSTON, C. G., and NOER, R. J. The treatment of adynamic ileus by gastrointestinal intubation. South. Surgeon, 1939, 8: 416.
23. SCHUMANN, E. A., and MISSETT, J. V. Observation upon adynamic ileus. Am. J. Obst. & Gynec., 1933, 26: 59–64.
24. STUDDIFORD, W. E. Spinal anesthesia in the treatment of paralytic ileus. Surg., Gynec. & Obst., 1928, 47: 862–865.
25. WAGNER, G. A. Zur Behandlung des Ileus mit Lumbaranæsthesie. Arch. f. Gynaek., 1922, 117: 336–339.
26. WANGENSTEEN, O. H. The Therapeutic Problem in Bowel Obstruction. Pp. 8–19. Springfield and Baltimore: Charles C. Thomas, 1937.
27. Idem. The Therapeutic Problem in Bowel Obstruction. Pp. 71–72. Springfield and Baltimore: Charles C. Thomas, 1937.
28. WANGENSTEEN, O. H., and PAINE, J. R. Treatment of acute intestinal obstruction by suction with the duodenal tube. J. Am. M. Ass., 1933, 101: 1532–1539.
29. WARD, ROBERTSON. An apparatus for continuous gastric or duodenal lavage. J. Am. M. Ass., 1925, 84: 1114–1117.

SUPERNUMERARY TARSAL SCAPHOIDS

EDWARD K. CRAVENER, M.D., F.A.C.S., and DONALD G. MacELROY, M.D.,
Schenectady, New York

THE extra scaphoid of the foot has instigated considerable investigation, since this small supernumerary bone, lying below (ventral) or medial to the scaphoid, is capable of and does cause symptoms. Its identity is frequently in dispute, because of its similarity to the sesamoids so often found in the feet. This, however, is not a sesamoid, for often it has a capsule and a cartilaginous joint surface.

The supernumerary bones arise in antiquity, and are correctly called "atavistic débris." Kidner has suggested that these may represent a sixth toe, as in the opossum. Jaboulay thinks that they may be epiphyses for the scaphoids, as the os calces have epiphyses. This cannot always be true, since, as mentioned, the adult extra scaphoid may have a true joint surface. Certainly, in the 2 month fetus the extra bones are a normal finding. For many years following this, the bone is lost until it becomes visible as an x-ray finding from the ninth year onward. Few children come to the anatomical laboratory, and we can obtain no valuable evidence concerning its existence in the early years of life. All extra scaphoids are not separated from the major mass of bone. We have seen a supernumerary scaphoid on one foot, while the contralateral foot showed nothing but an enlarged and hooked scaphoid. We feel that this is simply fusion of the two masses. Occasionally, the mass will be only partly fused, and a broken line will represent the old joint. If sufficient anatomical evidence could be obtained, perhaps we should find that all children have extra scaphoids, or perhaps some of the refractory flat feet are due to a supernumerary bone which cannot be shown by x-ray examination.

We have some evidence that it is found in families. We have seen it several times in mother

Fig. 1. Left, Extra scaphoid which presents some radiological evidence of localized Kohler's disease. Simple removal resulted in symptomatic cure.

Fig. 2. Supernumerary scaphoid where medial position resulted in a localized painful bursa.

Fig. 3. Left, A posterior type of supernumerary scaphoid. On removal of this extra scaphoid a true degenerative (hypertrophic) arthritis was found in the true joint line. Right, Extra scaphoid, fused to the main body. These are capable of producing all the symptoms attributable to extra scaphoids, except those due to degenerative arthritis.

and daughter, but never in father and daughter. It is impossible to get a familial series from x-ray findings alone, so these figures can only indicate and not prove a definite inheritance of this disorder.

How often does it occur? Again we must fall back on x-ray findings. Geist found that it occurred 14 times in 100 cases of presumably normal feet. We find it surprisingly often, but then our patients are x-rayed because of foot disorder, and do not have normal feet. It would seem worthless research to determine the exact number, for either the extra scaphoid causes symptoms or it does not. We know that it does not always cause pain, since we have found this adventitious inhabitant in roentgenograms taken for purposes other than painful feet.

Why does it cause symptoms? Here many theories are given and the majority abandoned. An early theory proposed by Monahan was that this bone developed in flat feet. This is simply the cart before the horse. Flat feet do accompany extra scaphoids, but probably as a result of the extra scaphoid. We have noted, but not proved, that these extra bones are found in the long, narrow foot. We have never seen them in a short broad foot, and this supports the theory that their presence is needed to support an evolutionary degenerating arch. Perhaps there is a grain of truth in this, or, conversely, the evolutionary degenerative arch is accompanied by these extra bones. We don't know. A third reason for pain is that the extra scaphoid initiates a bursitis by reason of a mechanical irritation. This does occur, and we have seen it. Kidner believes that the extra mass of bone pushes against the internal malleolus, causing pain. He further believes that adduction of the forefoot follows the attempt to escape this pressure, with the natural results of such adduction—flat-foot. The interesting theory of change at direction of muscle pulls and mechanical disadvantage are brought up, and on these are postulated some of the surgical treatments. Burman and Lapidus quote Kidner as stating that Kohler's disease may occur in this extra bone. They present a case which may confirm this. Finally, degenerative (traumatic) arthritis is mentioned as a cause of symptoms in this disorder.

It seems that the presence of extra tarsal scaphoids is sometimes accompanied by pain. Further, it has been shown that operative treatment relieves the pain, so it is logical to think that the supernumerary bones are a primary cause of

Fig. 4. Left, Partially fused extra scaphoid as shown by the incomplete joint line. Does this indicate that these fuse more commonly than is believed?

Fig. 5. Large extra scaphoid, which is fused to the body of the true scaphoid. The soft tissue mass over the medial posterior end of the scaphoid indicates a painful bursa.

tarsalgia. We feel that the pain here present must be divided into 4 categories. First, that resulting from faulty mechanics of the foot; second, that due to mechanical pressure from the shoes, as a bursitis; third, that pain which results from a traumatic synovitis of the posterior tibial tendon, as in deQuervain's disorder of the wrist, and finally, that arthralgia which comes from a degenerative arthritis in a mal-placed and adventitious joint.

The disorder, therefore, can be roughly grouped into 2 age periods—those disabilities of immature years and those of the degenerative phase of life. In childhood, refractory flat feet may be due to unossified extra scaphoids. Here the posterior tibial tendon is carried so obliquely as markedly to decrease its effective pull. We have seen such cases, in which the final diagnosis was made only after several years, and after effective identification of the ossifying extra scaphoid. Theoretically, such a mal-used extra scaphoid, in accordance with Wolff's law, should ossify early. Certainly, the presence of a bony mass which constantly impinges on the encasing shoe will cause bursitis and pain. The tenosynovitis, manifested by very localized pressure pain, will be found in the early age group, and in the later group if initiated by intolerable exertion. In the later group, despite the chronological age, degenerative arthritis in the mechanically inept joint may result and will cause pain on the slightest exertion.

Fortunately, in the major portion of life, that is, from the ninth year on, the extra scaphoid can be found on x-ray examination. Early, however, it cannot. But a well treated case of early refractory mid-foot pain should, after a few years, demand surgical investigation. In the proved case, the pressure of this mechanical impediment will demand intervention.

Several operations have been advised. Kidner, in 1929, suggested that the aberrant attachment of the posterior tibial tendon be transferred to the true scaphoid and the extra piece removed. Others believe that simple removal of the extra scaphoid is sufficient. We also are of the opinion that simple removal of the extra scaphoid or

scaphoids is effective. The tendon early attaches itself to the surgically traumatized area, and the slack is taken up by modifications of muscle pull. Such a simple procedure has resulted, in all of our cases, in symptomatic cure with bettered foot mechanics.

Finally, it must be remembered that an extra scaphoid is not always detached from the mother bone. The long-hooked process which represents a fused supernumerary bone will cause all symptoms, save those of localized arthralgia, that will a free extra scaphoid.

CONCLUSIONS

1. Extra scaphoids are not rare.
2. Certain of these will cause symptoms of, or predispose to, flat-foot.
3. Certain of these will develop a hypertrophic arthritis in their true joint space.
4. Certain cases of refractory flat-foot before the ages of 8 or 9 years are due to the presence of extra scaphoids.
5. These cases, despite the negative x-ray findings, should, after adequate conservative treatment, be explored surgically.
6. The painful bursitis, or the localized tenosynovitis concomitant with extra scaphoids, can be cured only by surgical repair.
7. The hypertrophic change, so common in the joints of these extra scaphoids, can be cured only by removal of the extra scaphoids.
8. The simple removal of the extra scaphoid and placement of posterior tibial tendon to a better mechanical position will, without further procedure, result in symptomatic cure.
9. The presence of a deformed, pain-producing scaphoid, even without extra bodies, is indication for a plastic repair.

REFERENCES

1. BURMAN, M. S., and LAPIDUS, P. W. Unusual appearance of the accessory scaphoid and the styloid epiphysis of the fifth metatarsal. J. Bone & Joint Surg., 1930, 12: 160.
2. GEIST, E. S. The accessory scaphoid bone. J. Bone & Joint Surg., 1925, 7: 570.
3. JABOULAY. L'epiphyse de l'astragale et l'epiphyse du scaphoide du pied. Lyon méd., 1889, 62: 482.
4. KIDNER, F. C. The prehallux (accessory scaphoid) in its relation to flat-foot. J. Bone & Joint Surg., 1929, 11: 831.
5. MONAHAN, J. J. The human pre-hallux. Am. J. M. Sc., 1920, 160: 708.

THE SURGICAL TREATMENT OF HYPEROSTOSING MENINGIOMAS OF THE SPHENOID WING

JAMES L. POPPEN, M.D., F.A.C.S., and GILBERT HORRAX, M.D., F.A.C.S.,
Boston, Massachusetts

THE meningiomas as a group as well as each individual type have become much better understood since the results of an exhaustive study of a lifelong experience were recorded by Cushing and Eisenhardt.[1]

In this presentation the authors wish to include only one branch of the meningiomas commonly known and spoken of by most neurosurgeons as the "sphenoid wing meningiomas." Limited still further will be the surgical considerations and technique for the removal of the *en plaque* tumor of the sphenoid ridge.

It is necessary to keep in mind the anatomy of the skull in the region of the sphenoid wing so that the symptoms produced by these tumors as well as the operative considerations may be more fully appreciated (Fig. 1). It is imperative for the surgeon to have a thorough understanding of the anatomical relationships, not only so that the actual removal of these tumors may be made less hazardous but also so that the roentgenograms may be properly interpreted.

No words could more adequately and briefly describe the sphenoid ridge than those used by Cushing. "Sharply demarcating frontal from middle fossa, a bony ridge curves outward on a horizontal plane from anterior clinoidal process toward the lateral aspect of the cranial chamber where it flares out to become lost in the pterional region of the cranial vault. The sphenoid ridge may be readily divided into three parts: (1) deep, inner or clinoidal; (2) middle or alar; (3) outer or pterional. The inner two-thirds roughly correspond to the posterior margin of the lesser sphenoid wing (ala parva); the outer third to the flaring margin of the greater wing (ala magna). To visualize properly the intracranial topography of the region requires exceptional three dimensional sense, for here come together the surfaces of three bony planes: (1) that of the orbital roof of an obliquely horizontal plane; (2) the roughly vertical aspect of the middle temporal fossa in a coronal plane; and (3) the vertical but obliquely placed outer wall of the orbit."

From the Department of Neurosurgery, The Lahey Clinic.

[1] Cushing and Eisenhardt. Meningiomas. Springfield, Ill.: Charles C. Thomas, 1938.

Since the symptoms depend greatly on the location of the point of origin of these tumors on the sphenoid ridge, Cushing saw fit to classify them as deep, middle, or pterional *en plaque* sphenoidal ridge meningiomas.

The deep or clinoidal tumor usually manifests itself subjectively by unilateral diminished vision and objectively by pallor of the optic nerve head and nasal hemianopsia. As it enlarges there is complete blindness on the involved side with homonymous defect in the other eye with possibly beginning or frank choking of the optic nerve head and complete primary atrophy on the tumor side. Exophthalmos occurs with bone erosion and invasion of tumor into the retrobulbar space, but it may occur from pressure on the cavernous sinus and subsequent venous engorgement. Because of the proximity of the superior orbital fissure, varying degrees of oculomotor palsies occur on the side on which the lesion is located. The most common nerve involved is the sixth, although complete ophthalmoplegia may develop. Local discomforts usually occur late. Other signs of local extension may be manifested by olfactory or gustatory hallucinations, mental changes, polydipsia and polyuria, and paralysis of the opposite side. Finally, the roentgenograms may show erosion or hyperplasia of bone.

In contradistinction to the deep or clinoidal tumors, the middle tumor first manifests itself by evidences of increased intracranial pressure and until it has attained such a size that extension across the midline occurs, as happens in some cases, no symptoms other than mental changes may be noted. The roentgenograms may demonstrate erosion, proliferation, or no change; therefore, studies with injection of air frequently have to be carried out to verify the site of the tumor.

The type of tumor most satisfactorily treated from the surgeon's standpoint is the pterional *en plaque* which I wish to discuss both as to the symptoms it produces and from a surgical aspect. The frequency of these tumors is demonstrated by the fact that only 19 were seen by Dr. Cushing in over 2,000 verified brain tumors. Peculiarly enough, all of the 19 occurred in women and Dr. Cushing knew of only 3 reported examples in

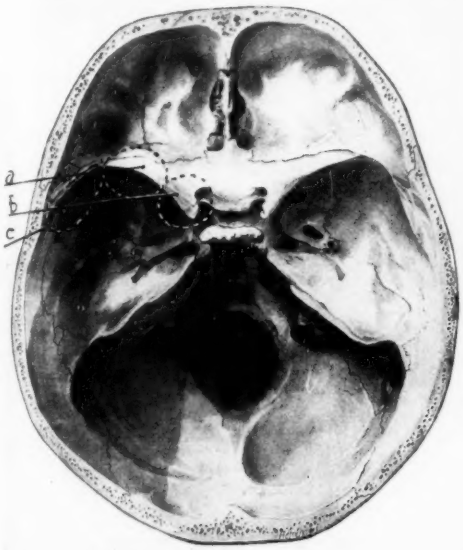


Fig. 1. Normal anatomy of base of skull in relation to the sphenoid wings. The circles outline approximately the regions from which sphenoid wing meningiomas arise most frequently. a, Alar; b, clinoidal; c, pterion. (From Spalteholz' *Anatomy*, Vol. 1.)

Fig. 2. Typical photomicrograph of sclerotic bone invaded by tumor cells.

men. In our group of 10 cases, 1 was a male (Case 5, Fig. 6). The diagnosis is readily made from a history of slowly developing exophthalmos with diminished vision on the affected side, swelling in the temporal region, frontal headache, and pain in the region of the orbit. The impairment of vision may occur late in the course of the disease; however, the frontal headaches and pains around the eye may be severe early and tend to decrease as the bone continues to become thicker. Varying degrees of exophthalmos may be found on examination, depending on the extent of the tumor. The affected eyeball may be only 2 millimeters or it may be many millimeters more prominent than the other eyeball. If exophthalmos is marked, the conjunctiva is congested and edematous. The exophthalmos is irreducible, non-pulsating, and displaced forward and downward. The optic nerve head is pale, with engorgement of the vessels. There may be fullness and tenderness of the temporal muscle (probably invasion of tumor into muscle).

Roentgenograms verify the diagnosis since they demonstrate an eburnation of the pterional region. In the very early cases (Case 4, Fig. 8), the anteroposterior and postero-anterior views are of particular value.

The hyperostotic effect of these tumors may be exceedingly great (Case 9, Fig. 9) and the production of soft tumor slight so that in many cases the latter is manifested only by a thickened dura with a thin layer of red granular tissue a few millimeters or more in thickness. A globular tumor was produced in only 1 of our cases. Why meningiomas of this type affect the bone in this way has been unexplained. The microscopic appearance of the *en plaque* meningiomas is fairly uniform (Fig. 2); in only a few the bone is so densely eburnated that no tumor invasion can be seen.

Even though it has been shown that this type of tumor is relatively uncommon, nevertheless it is one of the most important to recognize and treat early. It is notoriously slow in growth and therefore considerable hesitancy has been felt by many neurosurgeons in advising these patients to be subjected to early surgical intervention. Since a relatively incomplete removal often gave the

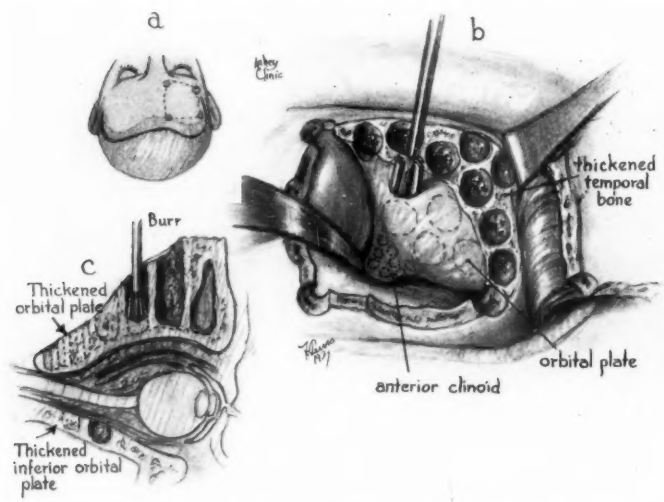


Fig. 3. a, Modified coronal incision with osteoplastic flap outlined. b, Greatly thickened pterional plate, orbital bone, and anterior clinoid; demonstrating multiple burr openings. c, Greatly thickened orbital plate and inferior orbital plate with outlines of burr openings.

patient years of relief, it was considered unwise to perform any radical procedure to remove the tumor. In advanced cases, the hazards of radical extirpation naturally increase and therefore as soon as the diagnosis can be made a wide removal of all the involved bone as well as the entire sphenoid wing and orbital plate should be executed.

Since in our experience the recession of the eyeball, after surgical treatment of malignant exophthalmos of thyroid disease, was directly proportional to the amount of internal decompression of the orbit, the technique described by Naffziger was modified by removing the sphenoid wing and lateral wall of the orbit as well as the orbital plate. These experiences introduced and systematized the technique now used in the hyperostosing sphenoid ridge meningiomas.

Briefly, the operation is performed by making a modified coronal incision (Fig. 3, a). The scalp is reflected anteriorly and a moderate sized frontal osteoplastic bone flap is turned down toward the temporal region, breaking it as low on the temporal muscle as possible. The dura is separated from the orbital plate posteriorly well over the greatly thickened sphenoid ridge, optic canal, and anterior clinoid, and also along the temporal bone laterally. The temporal muscle if not invaded with tumor is separated from the bone on the lateral surface of the orbit and pterional region. The thickened bone is now removed with giant rongeurs as deeply toward the triangle of the ala magna as possible. The greatly thickened and broad surface is honey-combed with the electric drill and the interlacing remnants of bone removed with rongeurs (Fig. 3, b). The orbital plate is then removed with the use of the electric drill and rongeurs, care being taken that the orbital capsule is not injured since if it is unintentionally opened, considerable embarrassment is experienced because of the protrusion of fat tissue. Since the inferior wall of the orbit as well as the lateral walls is also greatly thickened in the advanced cases, the burr can again be used to great advantage, the burr openings being made close to each other so that the partitions left may be readily removed with the rongeur (Fig. 4). In this manner all the bone may be removed from the orbital roof, side wall, and greater sphenoid wing to the superior orbital fissure. The portion of greatly thickened bone which covers the optic foramen and the greatly thickened anterior clinoid remain. In a few patients the hyperostosis over the anterior clinoid may resemble a turret and be 2 to 3 centimeters in thickness. It can be readily understood that if any of the vision is to be restored this bone must be removed, and this step naturally is the most

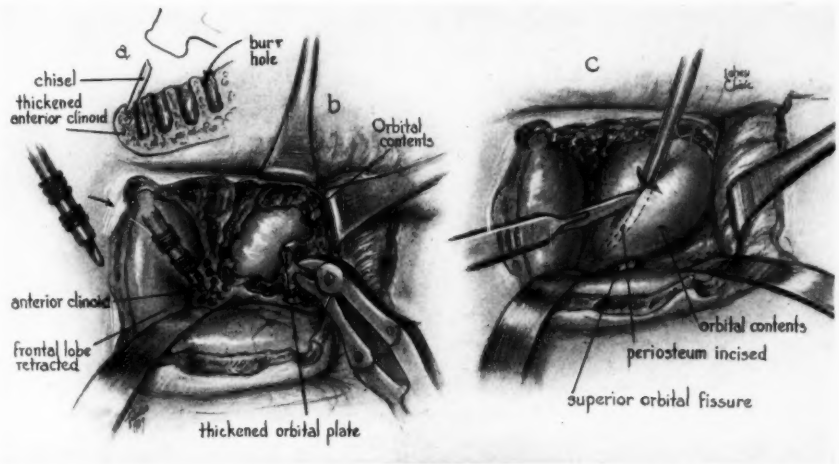


Fig. 4. a, Anterior clinoid greatly weakened by honeycombing with specially built burr which is electrically driven. Small fragments chipped away with mallet and chisel. b, Orbital periosteum and contents beginning to appear. c, Periosteum and orbital fascia incised. Demonstration of dura over temporal lobe and superior orbital fissure.

hazardous. To remove the bone safely, a special drill about 2 millimeters in thickness was made with an adjustable sleeve so that the depth could be readily gauged. With this drill attached to the electric motor many small openings are made 2 or 3 millimeters apart, within a few millimeters of the entire thickness of the bone. The greatly weakened structure is then removed by the judicious use of the mallet and chisel, small fragments breaking off without much jar or danger of breaking into a sinus. In this manner the entire anterior clinoid is removed, and the superior orbital fissure and optic canal are left well decompressed (Fig. 5, a). The orbital capsule is then widely opened and the intra-orbital tissues are allowed to protrude. They are examined for the presence of tumor. The incision should start over the annular ligament of Zinn and be carried upward, since in this way the protruding tissues do not interfere with completing the opening of the capsule. The dura is opened and if tumor is present it is removed or if only a thin, granular layer of tumor is present it is thoroughly eschared with electrocoagulation.

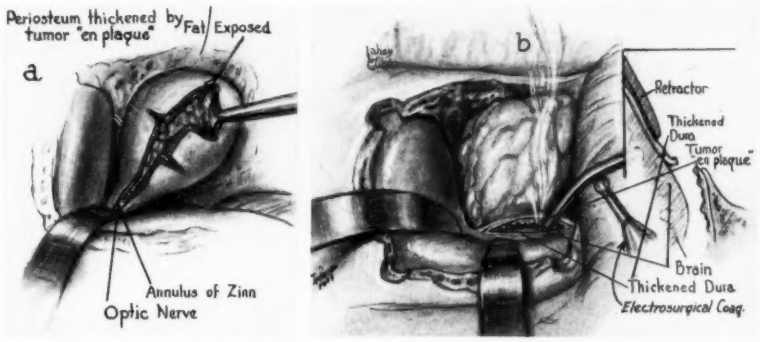
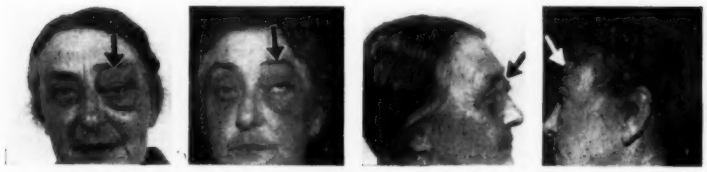


Fig. 5. a, Exposure of orbital contents by incision in periosteum. Demonstration of thin layer of tumor *en plaque* which may occur intra-orbitally as well as intracranially. b, Periosteum and tumor removed, showing herniation of orbital fat. Incision in dura at sphenoid groove demonstrating granular tumor being coagulated with electric surgical unit.



Case 1

Case 2

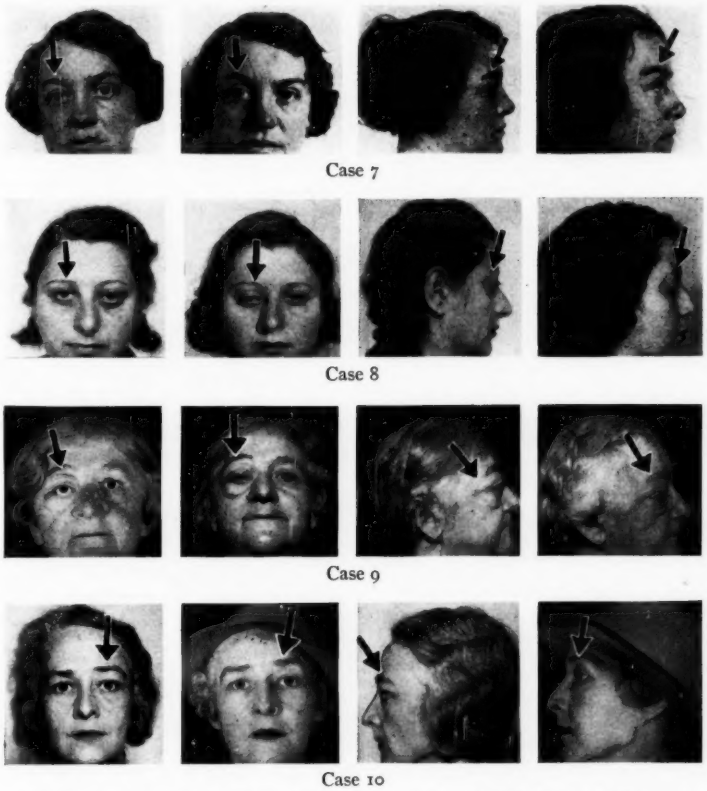
Case 3

Case 4

Case 5 Case 6

Fig. 6. Front and profile views of Cases 1, 2, 3, 4, 5, and 6 in this series both before and after operation with 2 exceptions. Case 5 is shown only before operation which terminated fatally from meningitis. In Case 6 only the photographs taken after operation are available. Cases 3 and 5 demonstrate the advanced stages.

In conclusion, emphasis should be placed on the fact that every patient with unilateral exophthalmos should have a thorough physical and neurological examination, including roentgenograms of the skull, to verify the diagnosis of pterional *en plaque* meningioma. Early complete removal of involved bone and dura is the procedure of choice. This surgical procedure has been illustrated and advised as a practical method and is used in our department at the present time. Since formerly incomplete operations were carried out with long periods of relief even though the cos-



Case 7

Case 8

Case 9

Case 10

Fig. 7. Front and profile views of Cases 7, 8, 9, and 10 both before and after operation. Case 9 demonstrates the advanced stage.

metic results were not noteworthy, it is fair to assume that by the procedure outlined satisfactory cosmetic results as well as permanent relief of visual disturbances from tumor will be afforded the patient. Ten brief case reports are submitted, with photographs taken before and after operation. The photographs and roentgenograms may be readily compared (Figs. 6, 7, 8, and 9).

CASE REPORTS

CASE 1. A woman, aged 62 years, was admitted to the clinic on October 11, 1937, and was discharged on November 8, 1937. The patient first noted protrusion of the left eye in 1917. This very slowly increased and she was finally operated upon by Dr. Harvey Cushing in 1929. Some subsidence of the eye followed the operative procedure but gradually protrusion again occurred and was accompanied by a gradual loss of vision so that for several years the patient has been practically blind in that eye. Her general health had been fairly good and there were no special complaints other than those noted.

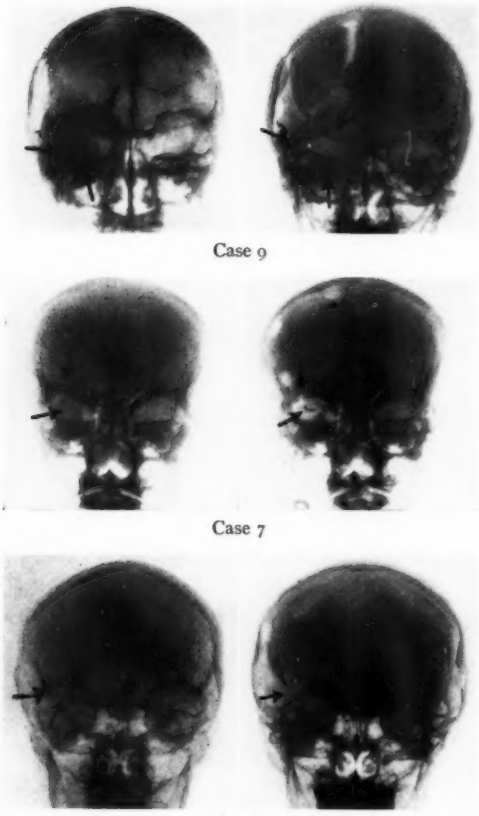
Examination revealed a marked protrusion of the left eye as compared with the right, with marked edema of the eyelids and soft tissues under the eye. The right fundus was normal; the left showed extreme atrophy. The exophthalmometer readings before operation were: base line, 99; right eye, 18 millimeters; left eye, 32 millimeters; acuity in the right eye was 20/20; in the left, nil. The right visual field was normal.

Operation was performed on October 14, 1937. A right transfrontal craniotomy was carried out with radical removal of greatly thickened and involved bone, muscle, dura, and tumor that invaded the orbital contents after the thickened orbital roof had been taken away.

The exophthalmometer readings following operation were: base line, 99; right eye, 18 millimeters; left eye, 17 millimeters. When last seen in February, 1938, the patient was doing well and improving.

CASE 2. A woman, aged 43 years, was admitted to the clinic on June 25, 1937, and was discharged on July 21, 1937.

The patient first noted protrusion of the right eye in March, 1937. She complained of headache in the right temporal region of 2 months' duration. She had no other



Case 9

Case 7

Case 4

Fig. 8. Anteroposterior roentgenograms taken before and after operation, demonstrating hyperostosing meningiomas of the sphenoid wing in Case 9, advanced, Case 7, moderately advanced, and Case 4, early stages. Compare with lateral views in Figure 9.

special complaints except that she had not felt very well for 2 years. There was no loss of vision.

Examination revealed a slight right exophthalmos. The exophthalmometer readings before operation were: base line, 101; right eye, 22 millimeters; left eye, 19 millimeters. The fundi were normal. Visual fields and acuity were normal. X-ray examination of the skull showed increased density of the right sphenoid wing as compared with the left.

Operation was performed on June 29, 1937. A transfrontal craniotomy was carried out with extensive removal of thickened and involved bone, including the roof of the orbit, together with removal of involved dura.

The exophthalmometer readings following operation were: base line, 101; right eye, 19 millimeters; left eye 19 millimeters. When last seen in February, 1938, the patient was in excellent condition.

CASE 3. A woman, aged 51 years, came to the clinic on July 7, 1937, and was discharged on August 7, 1937. The patient first noted protrusion of the right eye in 1932. This had at times progressed and at times receded somewhat. Vision had been poor in the right eye for many years. The patient's condition was followed for 5 years with repeated x-ray examinations of the skull. In May, 1937, the patient was seen for a second time by Dr. Cushing and because of an increase in the exophthalmos an operation was advised.

Examination proved negative except that of the eyes and x-ray films. There was a marked protrusion of the right eye and fullness of the right temporal region. The exophthalmometer readings before operation were: base line, 101; right eye, 28 millimeters; left eye, 16 millimeters. There was marked optic atrophy of the right fundus; the left was normal. Visual acuity in the right eye was 2/200; in the left, 20/20. Examination of the x-ray films showed great thickening and increased density of bone involving the orbital plate and contiguous sphenoid and temporal region.

Operation was performed on July 9, 1937. A right transfrontal craniotomy was carried out with removal of a meningioma that involved the bone over the orbit and the sphenoid region together with a large intradural meningioma which weighed 25 grams, for the removal of which it was necessary to take off the tip of the frontal lobe. Tumor was also present within the orbit.

The exophthalmometer readings after operation were: base line, 101; right eye, 18 millimeters; left eye, 16 millimeters. When last seen on February 8, 1938, the patient was very well. She had resumed her usual teaching position in September, 1937. The right eye had receded to normal.

CASE 4. A woman, aged 31 years, was admitted to the clinic on November 27, 1937, and was discharged on December 24, 1937. She complained of having had headaches in the left temporal and orbital regions and on the left side of the head since August, 1929. These had become progressively worse. She had noted a prominence of the left eye which had persisted for the same period. Patient also complained of having had double vision for 1 month before admission.

Examination revealed a definite exophthalmos on the left with widening of the palpebral fissure. The fundi, visual fields and acuity were normal. The exophthalmometer readings before operation were: base line, 96; right eye, 16 millimeters; left eye, 18 millimeters. Examination of the x-ray films revealed thickening and increased density of the left sphenoid wing.

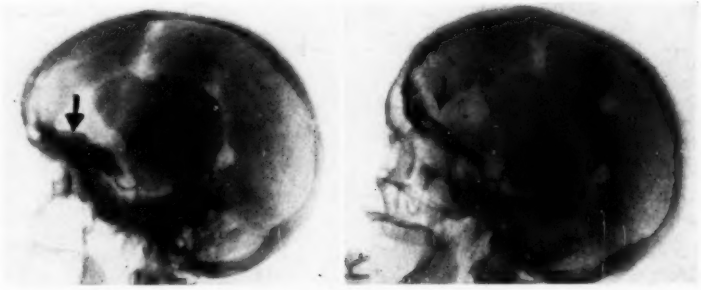
Operation was performed on November 29, 1937. A left transfrontal craniotomy was carried out with removal of thickened bone involved with tumor. No tumor was present in the dura.

The exophthalmometer readings following operation were: base line, 96; right eye, 17 millimeters; left eye, 16 millimeters.

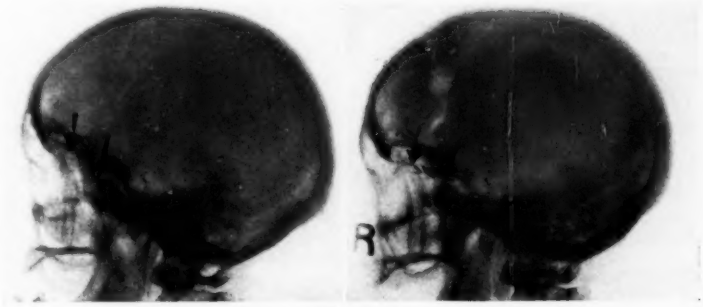
CASE 5. A man, aged 47 years, was admitted to the clinic on February 2, 1938, and died on March 14, 1938.

Patient complained of protrusion of the right eye of 11 years' duration. In 1926, he suffered an injury to the right side of the head. Shortly after this thickening of right frontal region was noted. A craniotomy was performed in 1929, at which time tumor and neighboring bone were incompletely removed. The eye gradually protruded after operation until, in 1937, it was easily dislodged from the socket. The patient had had 2 convulsions, 1 in April, 1935, and 1 in January, 1937. His health, otherwise, was good.

Examination revealed a marked protrusion of the right eye. Marked depression was present on the right as com-



Case 9



Case 7

Case 4

Fig. 9. Lateral roentgenograms taken before and after operation, demonstrating hyperostosing meningiomas of the sphenoid wing in Case 9, advanced, Case 7, moderately advanced, and Case 4, early stages. Compare with anteroposterior views in Figure 8.

pared with the left and there was marked prominence of the supra-orbital ridge on the right side. The general appearance of the disks was good; the right disk, however, was slightly atrophied. Visual acuity in the left eye was 20/30; in the right, 20/50; visual fields were normal. Examination of the x-ray films of the skull showed thickening of the right sphenoid ridge with increased density of the right sphenoid bone and adjacent frontotemporal bones. The right supra-orbital fissure was markedly narrow. The frontal bone was involved to the right margin of the frontal sinus.

Operation was performed on March 10, 1938. A recurrent meningioma was removed from the lateral region and temporal muscles. To accomplish its removal the orbit was unroofed and the frontal sinus was opened.

Death occurred, due to an acute meningitis which developed after operative removal of recurrent meningioma.

CASE 6. A woman, aged 46 years, was admitted to the clinic on March 12, 1937, and on May 9, 1937, and was discharged on March 22, 1937, and on June 19, 1937.

In March, 1934, beginning lacrimation of left eye was noted. In July, 1934, lacrimation continued and a begin-

ning protrusion of left eye was noted for the first time. In March, 1936, the patient was seen by Dr. Cushing. X-ray films of the skull taken at that time showed bony thickening, but no operation was advised. In January, 1937, the patient was again seen by Dr. Cushing. Some failure of vision in the left eye and further thickening of the bone were noted. Operation was advised.

Examination in March, 1937, was negative except for the eyes. There was an obvious protrusion of the left eye as compared with the right. The exophthalmometer readings before operation were: base line, 102; right eye, 17 millimeters; left eye, 25 millimeters.

The right fundus was normal; in the left, the disk outline was blurred and the disk was reddened. The visual fields were normal. Visual acuity in the right eye was 20/30; in the left, 20/40. Examination of the x-ray films revealed thickening of the bone of the orbital roof and lateral wall of the orbit as well as of the sphenoid wing.

Operation was performed on May 13, 1937 (postponed because of upper respiratory infection). A left transfrontal craniotomy was carried out with extensive removal of thickened bone. The dura was coagulated over a wide area, but it was not opened because tumor in the bone had involved the ethmoid cells and the latter had been opened at one point.

The exophthalmometer readings on June 18, 1937, were: base line, 102; right eye, 19 millimeters; left eye, 21 millimeters.

When last seen in December, 1937, the patient was in excellent condition.

CASE 7. A woman, aged 39 years, was admitted to the clinic on June 10, 1937, and discharged on July 1, 1937. She complained of headaches and progressive loss of vision in the right eye for 1 year and of easy fatigability.

Examination of the fundi revealed a right disk that was pale with primary atrophy; the left disk was normal. Visual acuity in the right eye was 5/200; in the left, 20/20. There was a marked right exophthalmos. The exophthalmometer readings before operation were: base line, 99; right eye, 21 millimeters; left eye, 16 millimeters. Examination of the x-ray films of the skull showed increased density of the right orbit and sphenoid wing and of the roof and lateral wall of the orbit.

Operation, which lasted 5 hours, was performed on June 15, 1937. The brain was under considerably increased pressure, the relief of which necessitated taking off the tip of the frontal lobe. Radical removal was done of all thickened, tumor involved bone, except where the internal carotid vein ran through it. Extirpation of a large intradural tumor was carried out. This was followed by a transfusion.

The exophthalmometer readings on July 14, 1937, were: base line, 97; right eye, 19 millimeters; left eye, 18 millimeters.

When last heard from in a letter dated July 30, 1937, patient expressed desire to begin work.

CASE 8. A woman, aged 36 years, came to the clinic on July 13, 1938, and was discharged on August 16, 1938. Patient complained of protrusion of the right eye of 6 years' duration and a discharge from both eyes for 2 years. Since April, 1938, she had had some diminution of vision in the right eye.

Examination revealed a definite right exophthalmos, partial ptosis of the right lid, and paresis of the right third and sixth nerves. The right fundus was moderately atrophied. The exophthalmometer readings before operation were: base line, 106; right eye, 20 millimeters; left eye, 18 millimeters. Visual acuity in the right eye was 20/70; in the left, 20/30.

Operation was performed on July 14, 1938. A right frontal craniotomy was carried out with complete extirpation of a sphenoidal wing meningioma and thickened and tumor involved bone; the involved dura was coagulated.

The exophthalmometer readings after operation were: base line, 106; right eye, 20 millimeters; left eye, 19 millimeters. Visual acuity in the right eye was 20/100.

When last seen on June 4, 1939, the patient reported that she had resumed her teaching position on February 1, 1939. She was feeling much better; the mild chronic infection of the eyes was about the same.

CASE 9. A woman, aged 55 years, came to the clinic on October 23, 1933, and was discharged on November 15, 1933. This patient had been operated upon by Dr. Harvey Cushing in November, 1928, at which time bone involved with tumor was partially removed. A gradual recurrence took place which resulted in further protrusion of the right eye with considerable conjunctival edema.

Examination revealed a marked prominence of the right eye with lacrimation, conjunctival edema, and edema of the eyelids. The right eye was blind, with marked primary atrophy. Movements of right eyeball were limited in all directions. In the left eye the fundus and visual acuity were normal. The exophthalmometer readings before operation were: right eye, 31 millimeters; left eye, 15 millimeters.

Examination of the x-ray films revealed an extremely marked thickening and density of the orbitofrontal region.

Operation was performed on October 28, 1933. A right transfrontal craniotomy was carried out with extensive removal of extremely thick and indurated tumor involved bone and unroofing of the orbit.

The exophthalmometer readings on November 11, 1933, were: right eye, 28 millimeters; left eye, 15 millimeters.

When heard from on June 7, 1935, patient stated that with the right eye alone she can now see to get around the house.

The exophthalmometer readings on June 7, 1935, were: right eye, 27 millimeters; left eye, 15 millimeters; on December 2, 1937, base line, 99; right eye, 30 millimeters; left eye, 15 millimeters.

Operation was again performed on March 11, 1938. A right frontal exploration was done with extensive evacuation of a recurrent meningioma in the bone and within the orbit.

When last seen on April 12, 1939, the patient felt well and the right eye had receded to normal.

CASE 10. A woman, aged 43 years, was admitted to the clinic on June 16, 1939, and discharged on July 17, 1939.

The patient complained of progressive prominence of the left eye for 6 years and headaches for 3 years, which had become progressively worse. Otherwise health was good.

Examination revealed an exophthalmos of the left eye. The exophthalmometer readings before operation were: base line, 94; right eye, 12 millimeters; left eye, 19 millimeters. The visual fields showed a slight temporal defect in the left eye. Examination of the x-ray films revealed a large sclerotic bony left sphenoidal wing.

Operation was performed on June 18, 1939, and removal of all sclerotic bone was carried out.

The exophthalmometer readings following operation were: base line, 94; right eye, 12 millimeters; left eye, 10 millimeters.

When last seen on July 21, 1939, the patient had made a complete recovery.

CAUSES OF DEATH IN CANCER OF THE CERVIX UTERI

LIONEL S. AUSTER, A.B., M.D., and ANGELO M. SALA, A.B., M.D., New York, New York

IT has long been our conviction that, with relatively few exceptions, patients harboring malignant neoplasms do not die directly as a result of their cancers. The cancer process initiates a succession of circumstances which eventually kill by secondary pathological manifestations rather than by the primary disease. Unless such secondary effects occur, usually as a result of contiguously invasive or disseminated metastases attacking some vital organ and interfering with its normal function, the patient may live in relative comfort for many years. The short course in cervix cancer is commonly the result of early involvement of neighboring important structures. This study was prompted by the realization that, except in a few major centers handling large volumes, these facts are not adequately recognized. It is presented with a point of view opposite to that usually encountered, in that the data are those of cases in which therapy failed, resulting in death.

This analysis is based upon a review of 1,558 cases of cervix disease seen at the New York City Cancer Institute from 1927 to 1938. In this group were 802 recorded deaths in the institution. Soon after the beginning of our study it was realized that such a mass of material including many incomplete records is of less value than a detailed analysis of the 124 cases for which full autopsy protocols are available. Therefore, although the entire group forms a basis for impressions and judgment as to clinical course, management, and relative values of therapeutic techniques, statistical analysis is made of only the smaller group which represents a cross section of all cases and includes examples of all types.

Primary treatment in these cases was carried out not only at the Institute but by the staffs of the other metropolitan clinics as well as by private practitioners. A comprehensive view of the late results following all types and techniques of treatment is thereby obtained.

AGE AND INCIDENCE

The total number of new admissions for the 10 year period was 13,454 of which 7,292 were women. The 1,558 cases of cervix disease represents 11.8 per cent of total admissions and 21.4 per cent of female admissions. This forms the largest single group of admissions classified under any one anatomical subdivision and represents an incidence of malignant disease found in women equivalent to diseases of the breast.

Of a total of 124 cases, 74 patients, or 59.5 per cent, were white and 50, or 40.5 per cent, were colored. Considering the relative proportion of white to colored population in New York City (20 to 1) this is an unusually high degree of incidence in colored women. It must be realized in this connection that our admissions represent exclusively cases in indigent patients, the majority of whom have well advanced disease when first admitted either to our clinic or to other hospitals from which transfer to us was made.

It is notable that the greatest number of patients—40 or 32.2 per cent—are in the fifth decade, between ages 41 and 50. The fourth and sixth decades have the next highest groups—24 and 23 per cent. Four per cent of the cases were seen in the age group 71 to 80 and 8 per cent each fell into the third and seventh decades.

No specific etiological factors were ascertainable. Practically all of the patients were married or had been sexually active. Most of them had had children. Nineteen cases, or approximately 15 per cent, had positive Wassermann reactions. Although accurate religious or racial data have not been collected, it is believed that in the entire group of 1,558 cases, 3 of the patients were Jewish women of whom 2 at least had lived with uncircumcised men.

DURATION OF DISEASE

The figures given in this section are not the same as data based upon a series reported for therapy evaluation since our cases represent only deaths.

It is significant that in general the longest length of life, after discovery of the disease, occurred in patients who appeared for examination and treatment shortly after the onset of symptoms. The largest number of patients are found to have been under our observation and care for less than 3 months before death. Forty-one, or approximately 33 per cent, of the patients were with us for 1 month or less. Twenty-three

From the New York City Cancer Institute and Hospital.
Presented before the Third International Cancer Congress, Atlantic City, New Jersey, September 15, 1939, and the New York Academy of Medicine, Section on Obstetrics and Gynecology, April 23, 1940.

patients were under observation and treatment by us for from 1 to 2 years. The total duration of the disease from onset is relatively short. The average length of life is 16.7 months, excluding one 10 year case. Twenty-six lived 1 year, 12 lived 2 years, 10 lived 3 years, and 5 lived 4 years. The majority died within 18 months.

Twenty-one per cent of the patients appeared for treatment within 3 months of the onset of their symptoms. An almost equal number delayed medical consultation for 6 months. Thirty patients, or approximately 25 per cent, did not seek advice for a year after they noted symptoms of some pelvic or vaginal disorder. These figures indicate delay as the chief reason for the high, rapid mortality.

NATURE OF SYMPTOMS

The outstanding feature of clinical symptomatology in cervix cancer is vaginal bleeding. Continued or intermittent hemorrhage was noted by 108 patients, or 88 per cent. Of these 4 patients described postcoital incidence. Eight per cent described purulent vaginal discharge as their outstanding symptom, which in almost all cases eventually became bloody. Discharge associated with recurrent bleeding incidents was noted in 11 cases, or 9 per cent. Although pain as a primary major symptom was relatively infrequent, abdominal pain was noted as an associated symptom in 7 per cent of the cases. These were usually patients harboring pelvic infection. Leg or thigh pain occurred in patients with perineural lumbar plexus involvement by neoplasm, or as a result of direct neoplastic invasion of pelvic bones, similar to the lesions in late prostatic cancer.

SURGICAL INTERVENTIONS

Some patients had accidental discovery of disease incidental to other operations. In general, surgical operative treatment was ineffectual in controlling the course of the neoplasm. There were 7 cases in which supracervical hysterectomy had been performed. It is not known which of these cases represent primary stump cancer following operation for myomas or which ones represent postoperative recurrent or residual disease after surgery performed as part of a combined therapeutic program for attempted cure.

We have encountered instances of attempted relief of the urological complications in late pelvic cancer, of which 5 examples are included in this series. In view of the extent of disease necessary to produce lesions requiring such surgical relief as nephrectomy or ureterostomy, we have concluded that such palliative surgery is contraindicated since it adds a further problem in the already complicated management and does not add to the patient's comfort or length of life.

CLINICAL STATE UPON ADMISSION

Clinical classification of cervix cancer in our institution is in accordance with the League of Nations plan based upon the following criteria:

Stage I represents the early lesion with only cervix involvement; stage II presents extension to vaginal epithelium with infiltration of one or more of the fornices; stage III presents parametrial or pelvic invasion with uterine fixation; stage IV describes the so called frozen pelvis with diffuse pelvic infiltration by a solid mass and obliteration of landmark structures or widespread and distant metastases of other types. Stage II plus is a subsidiary classification in which fall those cases of early, usually unilateral, parametrial extension without uterine fixation.

Stage III involvement was noted in 49.2 per cent of patients upon admission and 30.4 per cent were already in stage IV. Almost 80 per cent of patients were therefore in a markedly advanced stage of the disease before their symptoms became severe enough to cause them to seek medical attention, despite the fact that the local cervical condition was usually then noted to be well advanced in various stages of necrotic ulceration and bulky tumefaction. Apparently the local disease process may be well under way and may have produced marked pelvic extension without subjective evidence or symptoms causing great discomfort or inconvenience. This again indicates the necessity for educational measures designed to emphasize the importance of personal hygiene and an appreciation of the significance of presumably unimportant vaginal bleeding or discharge.

Except in obviously terminal cases, it has been the practice to treat these patients with either high voltage radiation or radium, or both. Considering the analysis of duration of disease, it is manifestly hopeless and irrational to attempt curative therapy in far advanced cases. Radiation, however, has been used as a satisfactory palliative measure for the control of hemorrhage. For this reason it has been used in most cases.

In our series only 1 case was in stage I, 12 cases, 9.7 per cent, were in stage II, and 10 cases, 8.2 per cent, in stage II plus. Two cases showed no clinical evidence of disease on admission.

PATHOLOGICAL DIAGNOSIS ON ADMISSION

One hundred and twenty-two cases were found to be squamous carcinoma and 2 cases showed

adenocarcinoma upon admission, either by biopsy or examination of slides prepared upon a previous admission at another institution. Not all specimens were graded, although in recent years the attempt was made to so classify the tumor sections. Most of these were grades II and III. It has been found, however, that the infection and necrosis present in most tissues from advanced cases make grading unreliable if not impossible. Despite a presumed relationship between the grade of the tumor, its radio-sensitivity and its subsequent course, we have been unable to justify any evaluations of degree of relative malignancy on this basis in cervix carcinoma. Even fairly well advanced, clinically stage II, pathologically grades I, II, and III lesions will respond locally in a satisfactory manner to topical radium and in many instances superficially heal completely. The patient's death, however, is inevitable as a result of the disseminated disease which, when well advanced at the onset of treatment, cannot be controlled in its course through the retroperitoneal lymphatics and in its massive infiltration in the pelvis.

It may not be out of place to mention the necessity sometimes of multiple biopsies from different areas or at different times in order to make an accurate original diagnosis or to evaluate progress of therapy or recurrence. One examination of necrotic tissue from a crateriform ulcer, for example, may not be sufficient to establish a correct diagnosis. Biopsy must be repeated until all reasonable doubt of a negative report is dissipated.

OCCURRENCE OF FISTULAS

Although direct invasion of the bladder and rectum with fistula formation is not a necessary precursor of urinary and peritoneal sepsis, the unusually high incidence of fistulous complications in many instances speeds up the progress of the disease by directly introducing a serious uncontrollable situation. There were 37 cases in which vesicovaginal and vesicorectal fistulas were noted. Although only 4 were noted upon admission, the often rapid supervention of this complication and its demonstration at autopsy within a relatively short time indicates that the presence of these fistulas is more frequent than is clinically realized. The fact that 30 per cent of these patients harbored such abnormal communications has led us to speculate upon the reasons for their occurrence. The fistulas are not always simple single tracts between the bladder or rectum and vagina. Numerous instances of complicated multiple fistulas involving various combinations of bladder, rectum, uterus, ureters, and vagina have been found.

One would expect to find that the usual cause for their occurrence is neoplastic invasion by direct continuity. Seven cases of the 37 were untreated by any means during the course of the disease. Two patients were initially treated only by operation; in 1 the fistulous complication was presumably the indirect result of operative trauma.

A discussion of the relative values of various forms of radiation therapy is not germane to the subject of this communication, and a detailed study of these aspects of the problem is reserved for a subsequent paper. Despite the fact, however, that the present material does not statistically completely substantiate all our impressions, we have always felt and still maintain that the rapid administration of high radium dosage intravaginally has a deleterious effect and predisposes to fistula formation to a greater degree than does the slow or French technique utilizing a smaller amount of radium over a longer period of time. Our figures show 5 cases of fistula in patients treated by rapid or "bomb" radium and 11 cases in patients treated by the slow method. Twelve cases treated by high voltage radiation alone without radium developed fistulas. Although these figures are paradoxical, it must be remembered that the rapid technique is used in only two institutions in New York and these cases form a relatively small proportion of the total.

ANTEMORTEM SYMPTOMATOLOGY

In contrast to the outstanding symptom of hemorrhage and discharge noted at onset, the chief symptom or state observed clinically during the month before death was sepsis. Seventy-one cases, 57.1 per cent, had evidence of profound toxemia, infection, and fever as the outstanding feature of the terminal course. Seven other patients manifested this state in sufficient degree to have it noted as an important secondary factor. Hemorrhage of severe character was seen in 17 cases, 13.2 per cent, with 5 more cases presenting this feature as an important concomitant symptom.

Many patients manifested no specific symptomatology other than weakness, stupor, anemia, and general debility. These have been grouped under the heading of cachexia, primary in 12 cases, 9.6 per cent, and secondary in 9, 7.3 per cent.

Cardiorenal failure was diagnosed in a total of 13 cases, 10.4 per cent, while intestinal and

abdominal symptoms predominated clinically in 6 cases, 4.8 per cent. Other symptoms, such as dysuria, rectal dysfunction, pulmonary infections, and diabetes accounted for the remainder.

ACTUAL CAUSE OF DEATH

It is no reflection upon the clinical acumen of the resident staff officers in their evaluation of the actual terminal situation of these patients at death to find that although the clinical diagnosis is generally accurate, the true specific pathological cause of death was frequently overlooked, unappreciated, or at least unnoted. There are several reasons for this, chief of which is the fact that these patients are usually in such bad state at death that it is difficult to determine all the facts accurately. Cardiac failure and pulmonary edema are common and pneumonia, which may clinically be an outstanding fatal symptom, is seen pathologically to be more often merely one of the terminal manifestations of a generalized septic process.

Table I summarizes the actual clinical and pathological findings in 124 cases. Attempt has been made to list both the primary or chief cause and the outstanding associated secondary conditions found.

In 92 cases, 74 per cent, *sepsis* is the chief pathological diagnosis. A breakdown of this group shows that there are 4 main subdivisions (Table I).

Local sepsis (which includes vaginopelvic ulceration, abscess, parametritis, infected ulcerated fistulas) was an associated finding in 75 cases, 60.6 per cent, but was found to be extensive enough to be listed as a primary cause in 17 cases, 13.2 per cent.

Peritonitis accounted for 18 deaths, 14.5 per cent, with 2 cases, 1.6 per cent, listed as a secondary state. This condition is seen to be a much more frequent and important terminal complication than hitherto believed and follows pyometra and pelvic abscess by direct extension through perforation of the uterus. Purulent infection with abscess formation in the uterus and adjacent pelvis was found in 20 cases. Interference with uterine drainage is the basic factor here.

There are two main causes for such occurrence. One group is usually seen following treatment in which the local cervix lesion may be controlled or even healed with the production of synechial adhesions in the vault of the vagina or closure of the cervical canal causing subsequent interference with uterine drainage. Pyometra supervenes and the lack of drainage *per vaginam* causes retrograde extension and perforation into the pelvis.

TABLE I.—ANALYSIS OF CAUSE OF DEATH IN 124 COMPLETE AUTOPSIED CASES

"Primary" cause as given is chief clinical diagnosis or major anatomico-pathological factor.
"Secondary" causes listed represent associated significant findings. Figures show number of instances.

	Clinical diagnosis				Pathological diagnosis			
	Primary		Secondary		Primary		Secondary	
	No.	Per cent	No.	Per cent	No.	Per cent	No.	Per cent
1. Sepsis	69	55.5	7	5.6	92	74.	79	63.7
a. Local (vaginopelvic ulceration, abscess, parametritis, fistulas, etc.)					17	13.2	75	60.6
b. Peritonitis					18	14.5	2	1.6
c. General (including endocarditis and blood stream infections)					28	22.5	0	
d. Nephrogenic					29	23.3	2	1.6
2. Hemorrhage and anemia	16	13.	12	9.6	10	8.	9	7.3
3. Uremia—renal failure	7	5.6	7	5.6	6	4.8		
a. Associated damage to urinary tract (e.g., hydronephrosis and pyonephrosis, etc.)							89	71.9
4. Pneumonia	14	11.3	8	6.4	6	4.8	38	30.7
5. Generalized distant metastases (beyond pelvis and retroperitoneal nodes)					5	4.	34	27.4
6. Cardiac failure and pulmonary edema	10	8.	8	6.4	3	2.4	27	21.8
7. Intestinal ileus					1	0.8	3	2.4
8. Embolism	1	0.8			1	0.8		
9. Shock	1	0.8						
10. Cachexia	6	4.8	2	1.6			20	16.
	Pyometra and pelvic abscess							
	"Frozen" pelvis (with or without necrosis)						57	45.8

The second main group is composed of those cases in which drainage is blocked by bulky tumefaction. A not inconsiderable number of patients present themselves with huge masses of tumor tissue filling the vagina, arising from the cervix. This tissue is a veritable carbuncle of carcinoma, composed of sponge-like overgrowth of tumor tissue, its interstices filled with pus and blood. The vagina is filled and the cervical canal occluded. Pyometra, parametritis, and pelvic abscess result. This is the one situation in which removal of the tumor tissue by surgical means is

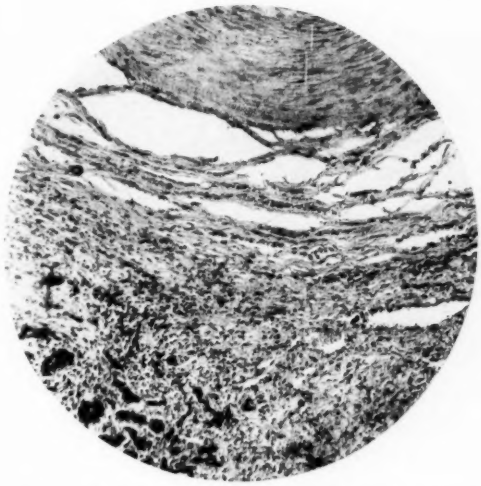


Fig. 1. Iliac artery showing invasion of perivascular lymphatics by carcinoma of cervix. N. Y. C. C. I., Autopsy XLI/37.

Fig. 2. Iliac artery showing invasion of perivascular lymphatics by carcinoma of cervix. N. Y. C. C. I., Autopsy XLI/37.

justifiable and necessary before the administration of radium or x-ray therapy. The bulk of the tumor may be readily resected under direct vision by means of the endotherm cutting current, with hemostasis by means of coagulation of the base. The cervical canal can then usually be identified and uterine drainage effected by the introduction of a tube through which the intrauterine abscess cavity may even be irrigated with hypochlorite solutions. Intra-uterine radium should not be introduced until the major infective process has subsided. We have 1 case in which death followed uterine perforation with peritonitis following radium introduction into an unrecognized pyometrial cavity. Occasionally radium applied to the cervix base intravaginally after resection of the bulk of the tumor as described will control the external lesion and make the cervical canal identifiable in cases in which this is previously impossible. Intra-uterine therapy may then be instituted.

Peritonitis is not only of the pelvic and low abdominal type but in about half the cases manifests itself as a diffuse, fibrinopurulent, plastic, exudative process. Unfortunately for accurate antemortem diagnosis, the peritoneal lesions are often clinically silent.

General sepsis is a term which includes endocarditis and blood stream infections, embolic abscesses of widespread distribution, typical splenic changes and other manifestations of generalized infection. This diagnosis accounted for 28 deaths, 22.5 per cent, and is listed as a subdivision to include those cases in which the infective processes were not specifically related to a single system although, of course, marked local or renal pathology, for example, may have been concomitantly present.

The largest single subdivision in the septic group, however, is formed by the 31 cases, 25 per cent, in which the major infective lesion was in the urinary tract.

Nephrogenic sepsis or *urogenic sepsis* is considered to be, for purposes of classification, that form of disease in which an overwhelming urinary tract infection is the major cause of death. In addition to this group, however, there is subgroup Table I, 3a, in which fall 89 cases, 71.9 per cent, in which associated damage to the urinary tract was present, in addition to some other specific major state. These figures are startling in that they indicate lesions of the urinary tract to be the most important single specific influence in the downhill path of patients dying of cervix cancer, for practically all of the patients in this study had some degree of urinary tract damage.

The pathogenesis of ureteral block and renal infection is seen as a result of two processes: one early and insidious, the second later and massive in its manifestations. In the earlier group it develops as a result of peri-ureteral lymphatic invasion by carcinoma cells traveling in the retro-

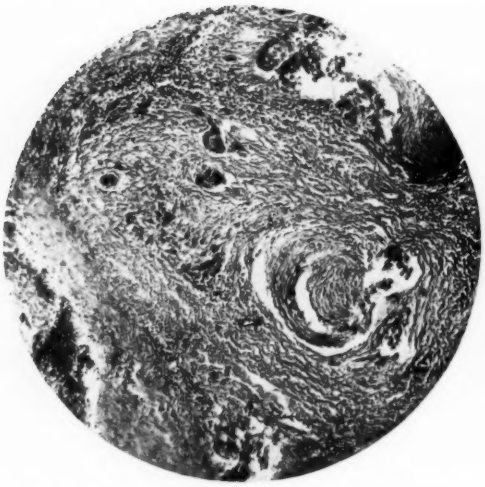


Fig. 3. Carcinoma of cervix—invasion of perivascular lymphatics. N. Y. C. C. I., Autopsy CLXV/36.

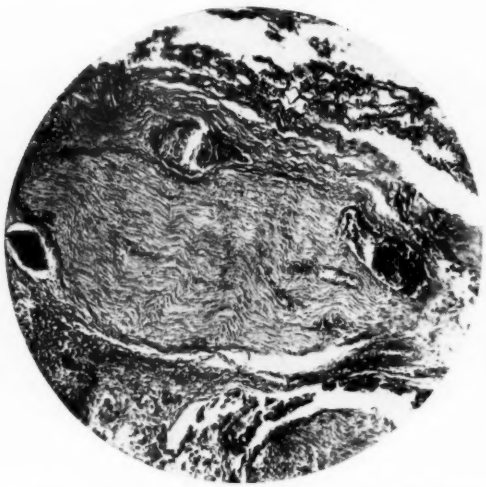


Fig. 4. Carcinoma of cervix—invasion of perineura lymphatics. N. Y. C. C. I., Autopsy CLXV/36.

peritoneal channels. Circumferential infiltration, constriction of the ureter, and ureteral mucous membrane damage are successive stages. The more obvious lesions, however, are the result of massive pelvic deposits with bladder and ureter infiltration and constriction. Interference with drainage and kidney function is a gradual process in which infection supervenes usually at an early period by the ascending route. Various degrees of cystitis, ureteritis, hydro-ureter and pyo-ureter, hydronephrosis and pyonephrosis, and pyelonephritis are seen. The tendency to renal failure without major infection is also manifest, although death by uremia is usually associated with some form of nephrogenic (or urogenic) sepsis, which in our classification takes precedence as a major specific cause of death. Although uremia (Table I, 3) alone is noted clinically in 14 cases, 11.2 per cent, in only 6 cases did it prove to be the outstanding lesion, since it is almost always associated with the urinary sepsis states.

It has been found that blood chemistry figures, except in terminal states, are not an accurate index to renal function in our material. This may be due to technical difficulties or to complicating factors as a result of other associated conditions. We have found, however, that intravenous urography provides a consistent means for evaluation of the progress of the pelvic disease. For about 5 years attempt has been made to follow all except obviously terminal cases by roentgenography of the urinary tract after the intravenous injection of excretory contrast media. In this way we have repeatedly been able to demonstrate gradual dilation of ureters and renal pelves and eventual anuria or non-functioning kidneys. Cystoscopy and ureteral catheterization have occasionally aided in establishing drainage following dilation of the ureter in its constricted portion. Such therapy must be instituted early to be of value. We have not found, however, that extensive urological operations designed to exteriorize urinary drainage are satisfactory or helpful, as far as the end-result is concerned.

It has occasionally been stated that ureteral block is the result of fibrosis following an extensive radiation program of radium and high voltage to the pelvis causing constriction of tissues about the distal end of the ureters. Our pathological studies have consistently demonstrated, however, that this is not so since all obstructive lesions of a constricting or compressing character have been found to be the result of neoplastic invasion with or without accompanying desmoplastic fibrosis. Photomicrographic slides of material dissected from these regions demonstrate the nature of the changes which occur (Figs. 1, 2, 3, and 4).

Even in cases in which direct ascending infection is not manifest on account of complete block or closure of the distal ureter lumen, it must be recalled that the high frequency of colon infection in these obstructed kidneys may result from bacterial invasion either directly from the bowel or

Fig. 5. Carcinoma of cervix—superficial healing complete. Deep down in the body of the cervix there was found a vessel containing carcinoma. N. Y. C. C. I., Autopsy CXXXII/35.

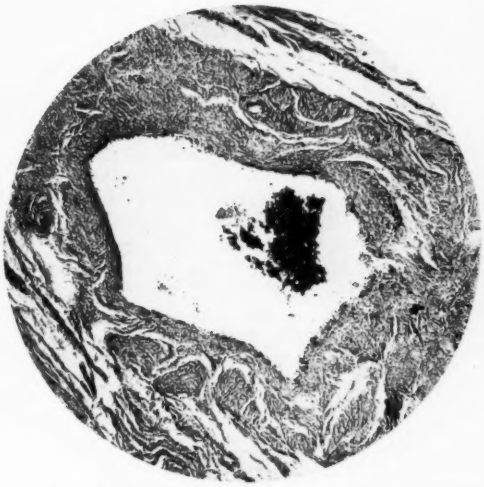


Fig. 6. Carcinoma of cervix—superficial healing complete. Deep down in the body of the cervix there was found a vessel containing carcinoma. N. Y. C. C. I., Autopsy CXXXII/35.

pelvic inflammatory lesions through the damaged wall or by way of retrograde lymphatic extension.

Hemorrhage and *anemia* account for 8 per cent of deaths on a primary pathological basis with an additional 7.3 per cent in which it was an important secondary factor. This comprises the second largest primary group pathologically, although from a clinical standpoint the combined primary and secondary diagnosis was made in 28 cases for a total of 22.6 per cent. This discrepancy in clinical and pathological findings indicates that although marked blood loss is an outstanding feature of the late course and even is frequently the precipitating fatal factor, it is more frequently considered to be an occurrence which results from the erosion of larger vessels in the course of a major ulcerative and septic process.

Although *pneumonia* was present in 38 cases, 30.7 per cent, as a secondary feature at autopsy, in only 6 cases, 4.8 per cent, was it considered to be the primary pathological diagnosis although death was clinically ascribed to it in 22 cases. In many of these cases a terminal lobular pneumonia is a concomitant part of a general sepsis or cardiorenal failure in patients weakened by long continued toxemia.

Generalized metastases, in which lesions were found beyond the pelvis and retroperitoneal nodes, were seen in an unusually high number of cases. In 34 instances, 27.4 per cent, metastatic dissemination was found in the liver, lungs, spleen, kidneys, bones, mediastinum, neck, brain. In 5 cases, 4 per cent, death was considered to be directly attributable to the effects of such distant dissemination. These were instances in which the lungs, pericardium, mediastinum, and heart were involved with the production of high vascular occlusion, hydrothorax and hemothorax and other associated lesions of the organs in the thoracic cage.

Cervix cancer has not commonly been considered as a source of widespread metastasis. Extensive thoracic and skeletal involvement occurred in our series in 8 cases. The most marked dissemination was seen in cases of long duration, this group including the 1½ to 10 year survivals. Apparently the reason that more instances of generalized metastases are not noted is because patients do not live long enough to have them. One patient, however, died with such dissemination in 8 months.

Involvement of the pelvic bones by direct invasion similar to the lesions in prostatic cancer was also noted.

The clinical diagnosis of *cardiac failure* and pulmonary edema was made in 18 cases, 14.4 per cent. Pathologically only 3 patients had their deaths attributed directly to this condition, whereas 27 patients, 21.8 per cent, were noted to have such associated pathology as a terminal

manifestation. *Intestinal ileus* due to intussusception accounted for 1 death. *Embolism* for another. Clinical diagnosis of shock in 1 case was found to be explained by peritonitis with perforation of the uterus following radium. Eight cases in which cachexia was indicated as a clinical diagnosis were all found to have other specific pathological conditions to account for their failure.

With very few exceptions almost all patients had varying degrees of pelvic infiltration. It is notable, however, that at death 57, 45.8 per cent, showed such infiltration to be extensive enough to be classed as "frozen pelvis" in which a mixture of inflammatory and tumor tissue completely filled the pelvis with obliteration of normal spaces and landmarks. Many of these solid infiltrations were the seat of varying degrees of inflammatory change, ranging from diffuse phlegmonous infiltration or cellulitis to large areas of necrosis with cavitation and varying forms of abscess formation. True pelvic abscess, however, was usually in association with pyometra by extension. It is our impression that many of the major necrotic areas may have been produced as a result of heavy radiation delivered to bulky infected tumor tissue.

POSTMORTEM PATHOLOGY

In carcinoma of the cervix, probably more clearly than in any other type of cancer, we see how and why unchecked cancer ultimately kills. Its pernicious spread is methodic, and, in the light of our experience at the autopsy table, predictable. No undiscovered toxin, presumably secreted by the carcinoma cell and poisoning the system, need be postulated. Carcinoma of the cervix kills because in its onward spread through anatomic routes it mechanically interferes with the physiological function of tissues and organs in its path. Treatment of the local condition is today hardly a problem for the therapist. Progress of the disease beyond the local area may well, and too often does, defeat his best efforts.

Permeation of the lymphatic spaces in the connective tissue, of which spaces the cervix has an abundance, is the chief method of advance. Perineural and perivascular lymph spaces are equally invaded. Invariably the periureteral lymph spaces are attacked, and if the patient does not die earlier for other reasons, she is bound to die from some effects of ureteral obstruction, usually with infection of the urinary tract. Invasions of the bladder and the rectum occur, but we have never been able to record either of these occurrences as the actual cause of death.

Periureteral invasion by carcinoma with constriction of the tube has been repeatedly found and demonstrated by us in both treated and untreated cases. In none of the treated cases have we had to attribute ureteral obstruction to fibrosis presumably brought about by the treatment; in our opinion, this is an over rated danger (Figs. 1 to 6).

Downward spread into the vagina and the less frequent but not rare upward advance into the corpus are also part of the advance by permeation of lymphatic spaces, but they have never proved to be death dealing complications except when pyometra has given rise to peritonitis.

In its spread to the pelvic tissues, carcinoma of the cervix does not spare the bones, if the patient lives long enough. Though blood borne metastases to bones occur, we feel that the most frequent bony involvement (i.e., involvement of the pelvic bones) occurs not by the blood stream but again by direct and lymphatic extension. A paper by Barany and Sala, soon to be published, deals with this specific problem.

Spread through lymphatic vessels with involvement of the lymph nodes occurs as a rule in cases in which the tempo of the growth has been retarded. We have seen in some cases of spread by lymphatic vessels a remarkable adherence to the course charted by the anatomy, where we have been able to demonstrate orderly progress of invasion of the nodes at the base of the broad ligament, and then the iliac, hypogastric, and sacral nodes, followed by the retroperitoneal, mediastinal, supraclavicular, and even cervical nodes. Cases have been found, however, in which the nearest nodes have been spared and metastases have been set up in more distant nodes, probably by tumor embolism.

Blood-borne metastases are nowadays not rare. We believe that they occur very late, and their more frequent occurrence is to be explained only by the fact that more patients are enabled to live long enough to get them.

SUMMARY

One hundred and twenty-four autopsied cases of cervix cancer have been analyzed.

There is a relatively higher incidence of this disease in colored women.

The greatest incidence is seen in the fifth decade. The average length of life of these patients was less than 17 months from onset as near as could be determined. The majority of patients died within 18 months. Half the patients seen had symptoms for 6 months and another quarter of the total number did not seek medical advice for a year.

Eighty-eight per cent of patients reported vaginal bleeding as the outstanding symptom.

Surgical operation, either for cure or palliation, was ineffectual in altering the course of the disease, except in the case of removal of bulky masses to establish uterine drainage.

Eighty per cent of patients were in clinical stage III or IV upon admission to our institution. No form of therapy can arrest the disease in these stages.

All except 2 patients had squamous carcinoma as shown by biopsy.

Vaginal fistulas, sometimes of complicated type, were present in 30 per cent of the cases. While many are the direct result of neoplastic invasion, we feel that some have been hastened or caused by treatment.

The chief antemortem symptoms or signs in these patients were manifestations of a septic state.

The outstanding cause of death in cervix cancer was sepsis either directly from, or secondary to, a local pelvic lesion. Chief groupings of the pathological diagnoses at autopsy are as follows:

1. Sepsis: (a) local—ulceration, abscesses, pyometra; (b) peritonitis—usually by direct extension through uterine perforation; (c) general—including blood stream infections; (d) nephrogenic (or urogenic)—in which overwhelming infection arises in the urinary tract.
2. Hemorrhage and anemia.
3. Uremia—renal failure.
4. Pneumonia.
5. Generalized distant metastases—beyond the pelvis and retroperitoneal nodes.
6. Cardiac failure and pulmonary edema.

Intravenous urography is the best method of demonstration and evaluation of renal function and ureter block. Damage to the urinary system occurs in almost all cases.

CONCLUSIONS

We believe that cancer of the cervix is amenable to successful treatment by radiation in various forms and combinations and the literature contains numerous authoritative and well substantiated reports of 5 year cures and over. Such results can be obtained only when adequate treatment is given to patients in the early stage of their disease and then continuous follow-up observation and treatment maintained.

To our best knowledge, there has been no previous attempt to evaluate accurately the causes of failure in the therapy and the real cause of death of the greater number of even presumably well treated patients.

Curative therapy is useless in clinical stages III and IV cases. Even though the local visible vaginal lesion may be banished and its recurrences controlled, most cases eventuate in necrosis with ulceration and severe local infection. The paramount difficulty in treatment is the control of the progressive damage to the urinary tract which is involved in almost all late cases. Superimposed infection results in an overwhelming majority of the cases and is the outstanding cause of death. Although infection of the urinary tract is the most important source of sepsis, peritonitis forms a large group which has not previously been sufficiently recognized since the process is frequently clinically silent.

Metastases of widespread character are not uncommon and should be noted more and more often in the future as therapeutic measures become more widespread in their application, resulting in longer life for these patients who, untreated, usually die within 18 months. Bone metastases, both of hematogenous skeletal distribution and of direct contiguous pelvic type, will be noted as patients live long enough to develop them. Thoracic lesions are also to be noted.

The most striking feature of this study, aside from the pathological findings, has been the realization that most patients come for treatment when they are already in an advanced stage and have had significant symptoms extending over from 6 to 12 months before seeking medical advice. With the remarkable progress that has been made in the techniques of therapy, the next step in the control of cervix cancer lies in the road of education—both lay and professional—to make both patients and physicians appreciate the possible significance of abnormal vaginal bleeding. Once the possibilities are appreciated perhaps they may be induced to do something about it.

PRIMARY PARTIAL GASTRECTOMY (PÓLYA TYPE) FOR DUODENAL ULCER

A Study of Results in 212 Cases

WALTMAN WALTERS, M.D., Sc.D., F.A.C.S., EVERETT B. LEWIS, M.D., and ROBERT G. LEMON, M.D., Rochester, Minnesota

ALTHOUGH partial gastrectomy for duodenal ulcer that is resistant to medical treatment has been almost a routine procedure in parts of Central Europe for many years, only in the past 9 or 10 years has this method of surgical management of duodenal ulcer assumed an important status in North America. It is desirable, therefore, to review the results of partial gastrectomy of the Pólya type performed at the Mayo Clinic for duodenal ulcer. Partial gastrectomy of the Billroth I type is not included in this review as this procedure is less commonly used and in the experience of one of us (Walters), it has not been so effective in the treatment of duodenal ulcer as has the Pólya operation. However, the results of a series of cases in which the Billroth I type of gastric resection was performed will be presented at a later time. Patients who had a gastroenterostomy or a partial gastrectomy performed at a previous time were not included in this series.

The indications for partial gastrectomy for duodenal ulcer are difficult to define. This is due to the fact that there are some surgeons who believe that partial gastrectomy should be done as a routine procedure for all patients who have duodenal ulcers that require surgical procedures. Such a viewpoint explains the higher mortality of partial gastrectomy than when an operation is chosen on the basis of the patient's general condition and the character of the duodenal ulcer, both as regards size, extent, and situation. We have attempted to evaluate results of partial gastrectomy performed for duodenal ulcer in a group of cases in which the condition of the patient, the size of the duodenal ulcer, and the mobility of the duodenum would indicate that a partial gastrectomy, removing, in most cases, more than half of the stomach including the pyloric sphincter muscle, the first portion of the duodenum and the duodenal ulcer, could be accomplished with sufficient duodenum remaining to be accurately closed, thus assuring that the operation might be done with reasonable safety; leakage from the duodenal stump is the operative menace.

The patients for whom we have thought the operation of partial gastrectomy for duodenal ulcer might be indicated were those in the third, the fourth, and the fifth decades of life; those who lead an active life, particularly from the occupational standpoint; those who, because of lack of will power or desire on the patient's part, had not been following dietary restrictions prior to operation; those who would not give up the habit of smoking and drinking alcoholic beverages, and those who had experienced hemorrhages from the ulcer. Consecutive partial gastrectomies in 212 cases form the basis of our investigation. In an evaluation of the results of any particular method of surgical procedure, it is important to make a comparison of the mortalities and results as well as the applicability of the procedure as compared with other surgical procedures.

A high mortality rate associated with partial gastrectomy is the basis for most of the criticism of the method. An operative mortality as high as 18 per cent has been reported from two clinics (5). However, these series included secondary operations which carry a higher risk than primary procedures. Lower figures for operative mortality have been presented by Finsterer (2 per cent in 357 cases, 1926); Still (4 to 5 per cent in 84 cases, 13 of which were of duodenal ulcer); Graham (3.8 per cent in 140 cases); Berg (6.9 per cent in 401 cases); and Lake (7 per cent in 242 cases). Many of the operations in these series likewise were performed for gastric ulcer and for anastomotic jejunal ulcer. Therefore, such figures do not accurately represent the operative risk of primary partial gastrectomy for duodenal ulcer.

Advocates of partial gastrectomy for duodenal ulcer have called attention to the low incidence of anastomotic jejunal ulceration and to the high percentage of good results that follows such a procedure. In this regard, also, there has been some variation in the experience of different

From the Division of Surgery, the Mayo Clinic.
Dr. Lemon now residing in Glendive, Montana.

TABLE I.—PRIMARY PARTIAL GASTRECTOMY FOR DUODENAL ULCER*

Pre-operative status	Operative technique	Total cases	Operative mortality			Follow-up						
							Condition					
							Good		Nausea, etc., p. o.; no symptoms of ulcer		Recurrent symptoms of ulcer	
			Cases	Per cent	Causes of death	Cases	Number	Per cent	Number	Per cent	Number	Per cent
Duodenal ulcer without previous ulceration	Posterior Pólya	144	3	2.1	1—Pulmonary embolism 1—Myocardial infarction 1—Bronchopneumonia; peritonitis?	134	109**†	81.3	21	15.5	4+	3
Duodenal ulcer with previous closure of perforation	Posterior Pólya	25	0	0		25	21	84.0	3	12.0	1	4.0
Gastric and duodenal ulcers, concurrently; without previous operation	Posterior Pólya	43	1	2.3	1—Pneumonia, peritonitis, and duodenal fistula	38	35	92.0	3	8.0	0	0
	Total posterior Pólya operations	212	4	1.9		197	165**†	83.5	27	14.0	5	2.5

*More than one-third of stomach removed.
**Includes 4 anterior Pólya-Balfour operations.
†Two died at home, but without symptoms of ulcer.
+Three had gastrojejunal ulcer, by roentgenologic examination; 1 had a recent hemorrhage.

clinics. In the reports previously referred to, the follow-up studies have been as follows: Lahey and Marshall observed excellent results in 84 per cent of cases, fair results in 9 per cent, and recurrence in 7 per cent; St. John and his associates noted good results in 90 per cent of cases; Finsterer observed cures in 94 per cent of 236 cases, improvement in 3.4 per cent of cases, and no cure in 2.1 per cent of cases; Still obtained good results in 90 per cent of cases after performing the Finsterer type of resection; Lake, in a series of 198 cases, found such treatment unsatisfactory in 15 cases, or 7.6 per cent; 3 cases of anastomotic jejunal ulcer occurred, less than 2 per cent; Berg, in a series of 516 cases in which primary and secondary operations were performed, found recurrence in 1.1 per cent of cases; Crile and Crile found, in a follow-up study of 20 cases, that gastric symptoms occurred after operation in 20 per cent.

Ogilvie found no recurrence after 100 partial gastrectomies in which the pylorus was removed, but 3 recurrences were encountered in 12 cases in which operation was performed for duodenal ulcer and in which the pylorus was not removed. This is in contrast to Finsterer's experience with 236 cases in which he observed cure in 94 per cent and recurrence in 2.1 per cent. As a rule, removal of the pylorus was not carried out by Finsterer. (1926).

In none of these reports is a clear distinction made between the results of primary partial gastrectomy for duodenal ulcer on the one hand and the results of partial gastrectomy for gastric ulcer and for anastomotic jejunal ulcer, on the other.

The present study includes 187 patients on whom primary partial gastrectomy of the Pólya type was performed for duodenal ulcer, during the period from January 1, 1929, to January 1, 1939, but 43 of these patients with duodenal ulcer had associated gastric ulcer (Table I). In most of these cases, operation has been performed in the past 6 years. It also includes 25 patients who had recurring duodenal ulcer following previous closure of acute perforations, on whom partial gastrectomy was performed at the clinic in this same period of time. For clarity, those patients who have not had a previous surgical procedure performed on the stomach or duodenum are separated from those who have previously required surgical closure of a perforated duodenal ulcer. In some cases of the latter group, a form of pyloroplasty may have been performed when the perforated ulcer was closed.

In addition, those patients who, at the time of operation at the clinic, were found to have a gastric ulcer as well as a duodenal ulcer are separated from those patients who had only a duodenal ulcer. No patient was included in this

TABLE II.—SUMMARY OF RESULTS OF GASTRIC ANALYSES MADE AFTER OPERATION IN 116 CASES

Pre-operative status	Operative technique	Free acid	Follow-up							
			Cases		Condition					
					Good		Nausea, cramping, etc.		Recurrent ulcer	
			Number	Per cent	Number	Per cent	Number	Per cent	Number	Per cent
Duodenal ulcer without previous operation	Posterior Pólya	Present	23	28	19	28.5	2	15	2	100
		Absent	59	72	48	71.5	11	85	0	
Duodenal ulcer with previous closure of perforation	Posterior Pólya	Present	3	20	2	14	No analysis		1	100
		Absent	12	80	12	86	No analysis		0	
Gastric and duodenal ulcers concurrently, without previous operation	Posterior Pólya	Present	7	37	7	41	0		No cases	
		Absent	12	63	10	59	2	100	No cases	

study unless a third of the stomach, or more, was removed. Although at least one-third of the stomach was removed in some of the earlier cases operated on several years ago, by far the largest number of patients have been operated on in the past 5 or 6 years and in these instances we have removed half and usually two-thirds of the stomach.

Recent clinical information has been obtained from 197 (95 per cent) of the 208 patients dismissed from the clinic. Information also is available in regard to results of gastric analyses made after operation in 116 (56 per cent) of the 208 cases (Table II). Except for those patients who reply that they are perfectly well, it is difficult in many instances to classify the state of health of the individual. It is obvious that a person who has many so called functional symptoms, for which an adequate organic cause was not found before operation, may not be relieved of these symptoms by partial gastrectomy. Hence, the patient may not feel perfectly well after operation, and yet he may have relief from the symptoms of duodenal ulcer and may represent a good result of surgical therapy.

This group of patients merges with another group in which there is no evidence of recurrence of the duodenal ulcer or of development of an anastomotic ulcer, and yet the patients are not entirely well. Fullness after meals, and nausea, especially after breakfast, are the most outstanding complaints. Other less frequent, but equally annoying, symptoms are sweating, especially after meals, fatigue, and lack of strength. These symptoms have been attributed to irritability of the vagus nerve and too rapid emptying of the gastric contents into a jejunum that is not prepared to receive such unmodified gastric contents. However, these symptoms also may occasionally follow performance of partial gastrectomy when the von Haberer modification of the Billroth I technique is used, after which the duodenum and not the jejunum receives the gastric contents. Most patients are able to obtain relief from these digestive symptoms by taking some care in regard to their dietary regimen and by lying down for a few minutes after eating.

It is interesting to observe in Table I that the best results occur among those patients who had a gastric ulcer associated with a duodenal ulcer.

In our series, partial gastrectomy of the Pólya type among patients who had had an acute perforation closed at a former operation was followed by about the same percentages of good results and failures, as was partial gastrectomy of the same type among patients who had not had former surgical procedures performed on the stomach or duodenum. In this small group of 25 patients, there were no postoperative deaths. Four deaths, an operative mortality of 1.9 per cent, among the 212 patients who had primary partial gastrectomy, is worthy of note. Two of the 4 deaths occurred following vascular accidents that, at present, are largely unpreventable. One patient died of peritonitis associated with a duodenal fistula and 1 patient died of bronchopneumonia, with some resolving peritonitis present at the time of death.

In regard to the posterior Pólya type of partial gastrectomy performed as a primary surgical procedure in the treatment of duodenal ulcer only, it is apparent that 97 per cent of 134 patients whose course was followed after the operation did not experience the development of another ulcer. The 134 cases do not include the 25 cases of partial gastrectomy in which closure of an acute perforation of the duodenal ulcer had been performed previously and the 43 cases of duo-

denal ulcer in which there was an associated gastric ulcer. Eighty-one per cent of the 134 patients were able to live a normal life without undue restriction of their diet and activities. Some restrictions of diet and activity were required by about 16 per cent of the 134 patients in order to remain reasonably well. In 4 cases, or 3 per cent, evidence of ulcer developed. In 3 of these 4, a gastrojejunal ulcer was demonstrated by roentgenological methods. The fourth patient has been periodically incapacitated by hemorrhages. All of these 4 have obtained some relief from a medical regimen.

SUMMARY

In the 212 cases in which the posterior Pólya type of operation was performed, the mortality was 1.9 per cent. Although this was a consecutive series of partial gastrectomies, it is not to be assumed that it was a consecutive series of patients operated on for duodenal ulcer, for in many cases the large size or the character of the ulcer or the condition of the patient seemingly would not permit a partial gastrectomy without excessive risk; therefore, gastro-enterostomy, gastroduodenostomy, or pyloroplasty was performed.

Anastomotic jejunal ulceration occurred in 2.5 per cent of the total of 197 cases followed after partial gastrectomy. After the operation, 83.5 per cent of patients were well without undue restriction of diet or activity. Fourteen per cent required restriction of diet or activity or both in order to remain in comparatively good health. Thus, a total of 97.5 per cent were without recurrence of ulceration after partial gastrectomy.

Of those patients on whom gastric analyses were obtained after operation, two-thirds to four-fifths of those without recurrent ulceration after operation had anacidity, and only rarely was a normal or greater than normal value for free acid obtained. When a jejunal ulcer was demonstrated, almost invariably greater than normal amounts of free acid were present.

REFERENCES

1. BERG, A. A. The mortality and late results of subtotal gastrectomy for the radical cure of gastric and duodenal ulcer. Ann. Surg., 1930, 92: 340–359.
2. CRILE, GEORGE, and CRILE, GEORGE, JR. Indications for and end results of surgery in the treatment of duodenal ulcer. Am. J. Surg., 1938, 40: 123–127.
3. FINSTERER, H. Discussion on the place of gastro-jejunostomy in gastric and duodenal surgery. Brit. M. J., 1926, 2: 557–559.
4. GRAHAM, R. R. The surgeon's problem in duodenal ulcer. Am. J. Surg., 1938, 40: 102–117.
5. LAHEY, F. H., and MARSHALL, S. F. The surgical treatment of peptic ulcer; based upon one hundred and thirty subtotal gastrectomies for peptic ulcer. New England J. Med., 1937, 217: 933–940.
6. LAKE, N. C. Partial gastrectomy; a review of 320 cases. Brit. M. J., 1937, 2: 49–53.
7. OGILVIE, W. H. The approach to gastric surgery. II. Ulcer of the stomach. Lancet, 1938, 2: 295–299.
8. ST. JOHN, F. B., HARVEY, H. D., GIUS, J. A., and GOODMAN, E. N. A study of the results of surgical treatment of peptic ulcer. Ann. Surg., 1939, 109: 193–218.
9. STILL, R. J. Mortality and later results of subtotal gastrectomy. Lancet, 1936, 2: 1030–1034.

EDITORIALS

SURGERY
Gynecology and Obstetrics

FRANKLIN H. MARTIN
Founder and Managing Editor
1905–1935

LOYAL DAVIS, EDITOR

Associates
SUMNER L. KOCH MICHAEL L. MASON

DONALD C. BALFOUR, *Associate, Editorial Staff*

AUGUST, 1940

CORONARY DISEASE AND SURGICAL THERAPY

THE article by Dr. Fauteux in this number of SURGERY, GYNECOLOGY, AND OBSTETRICS is evidence of the steadily increasing rôle of surgery in the treatment of disorders of the heart. The treatment of wounds of the heart, of suppurative pericarditis, and of chronic adhesive pericarditis, by surgical methods is firmly established and is generally accepted. Surgical attack upon the sympathetic nervous system in angina pectoris has already won its way as a useful method in a limited group of patients. The application of total thyroidectomy for heart failure is still in the experimental stage, and a final opinion as to its eventual place cannot be ventured. Ligation and division of a patent ductus arteriosus, as recently demonstrated by Gross, is a noteworthy contribution in the field of cardiac surgery.

In the last five years through the work of Beck, of Cleveland, and O'Shaughnessy, of London, a new attack upon coronary disease has been brought forward. These men have sought methods to improve an impoverished coronary supply by bringing blood to the myocardium through the establishment of an additional collateral circulation. They have demonstrated in animals that muscle grafts from the thoracic cage or fat grafts of a slip of omentum brought through the diaphragm may be laid on the heart; there may acquire firm adhesions; and, through these adhesions, may revitalize a poorly nourished myocardium. This effort has continued with human cases, and, in a few instances, there seems adequate proof that these procedures have been beneficial. Whether such procedures can be generally applied without great risk and how great a benefit can be expected is yet to be ascertained.

Now Dr. Fauteux brings forward a new contribution in the same field. Pointing to the advantages in peripheral surgery of ligation of the major vein whenever the major artery is damaged or must be sacrificed, he has carried this principle to the surgical treatment of coronary disease. Finding first a point on the ramus descendens of the left coronary artery of a dog at which resection was universally fatal, he demonstrated that the animal is saved if the companion vein is ligated at the same point simultaneously with the arterial resection. Moreover, his experiments show that ligation of the vein at this point protects the animal against ligation and resection of the artery, even when this latter procedure is carried out months later. He further discusses the similarity between coronary disease and femoral obliterative arterial disease, and draws the conclusion that, if resection of an obliterated femoral vessel and ligation of its

companion vein is good for the lower extremity, a similar procedure may be beneficial in coronary disease. He points out that the physical, as well as neurophysiological, interpretations of such a procedure are generally accepted in the field of peripheral vascular disease.

This is not the first time that such analogies have proved valuable, and certainly his experimental work justifies further endeavor along this line. As Sir James MacKenzie has said, the ingenuity of the surgeon may eventually overcome all obstacles in cardiac surgery, and certainly this contribution of Dr. Fauteux's is a challenge to all interested in the relief of a very common malady to man.

ELLIOTT C. CUTLER.

"FUNCTIONING" TUMORS OF THE OVARY

THE rather recent recognition of "functioning" tumors of the ovary with their characteristic trains of symptoms has furnished a chapter of lasting interest to the subject of gynecology. As a result of this knowledge new sign-posts have appeared in the diagnosis of certain gynecologic lesions and the treatment and prognosis of solid ovarian neoplasms have been improved materially. Even in the field of embryology these tumors have been revealing, too, for their structure has suggested why the ovary participates in the propagation of such a variety of neoplastic lesions.

From the primitive cells of the undifferentiated gonad there arises, through a process of cellular segregation or maldevelopment, the dysgerminoma. This tumor usually manifests itself in young individuals—more than 60 per cent of whom are more or less of a neutral or pseudohermaphroditic type. Amenorrhea or scanty menses are common symptoms; the external and internal genitalia usually are developed poorly, and the breasts are frequently small. All of these features reflect a general lack of sexual differentiation. When the tumors are examined pathologically, they frequently are found to be bilateral; they are almost always encapsulated, and of brain-like consistency. Cytologically they are composed of highly undifferentiated cells resembling those found in the gonads before the stage of sexual determination. To the pathologist these tumors are of unusual interest because they occur in both sexes and are identical with the seminomas of the testis. To the surgeon they represent the paradox of a highly malignant neoplasm which carries a good prognosis, sometimes even after local extirpation. To the roentgenologist they represent one of the most radiosensitive lesions known.

The ovary of every woman carries within its hilus a potential testis. Just what combination of factors decides the fate of this potentiality is a matter of conjecture, but certain it is that occasionally these rests develop into arrhenoblastomas—testicular tumors in otherwise healthy ovaries. Depending on the number of interstitial cells present, and consequently the amount of testosterone elaborated, this tumor gives rise to masculinization with sterility, a syndrome which is so well known that repetition is scarcely merited. Although lesions other than those of the ovary more often produce this syndrome, its presence in a young or middle-aged woman who harbors a solid ovarian neoplasm should be sufficient to warrant an abdominal exploration with the probability of arrhenoblastoma in mind. These tumors command the respect of the surgeon because of the rather startling clinical improvement following removal. Menses return, usually within a month; the normal female habitus is soon restored; pregnancy becomes possible. Occasional recurrences are

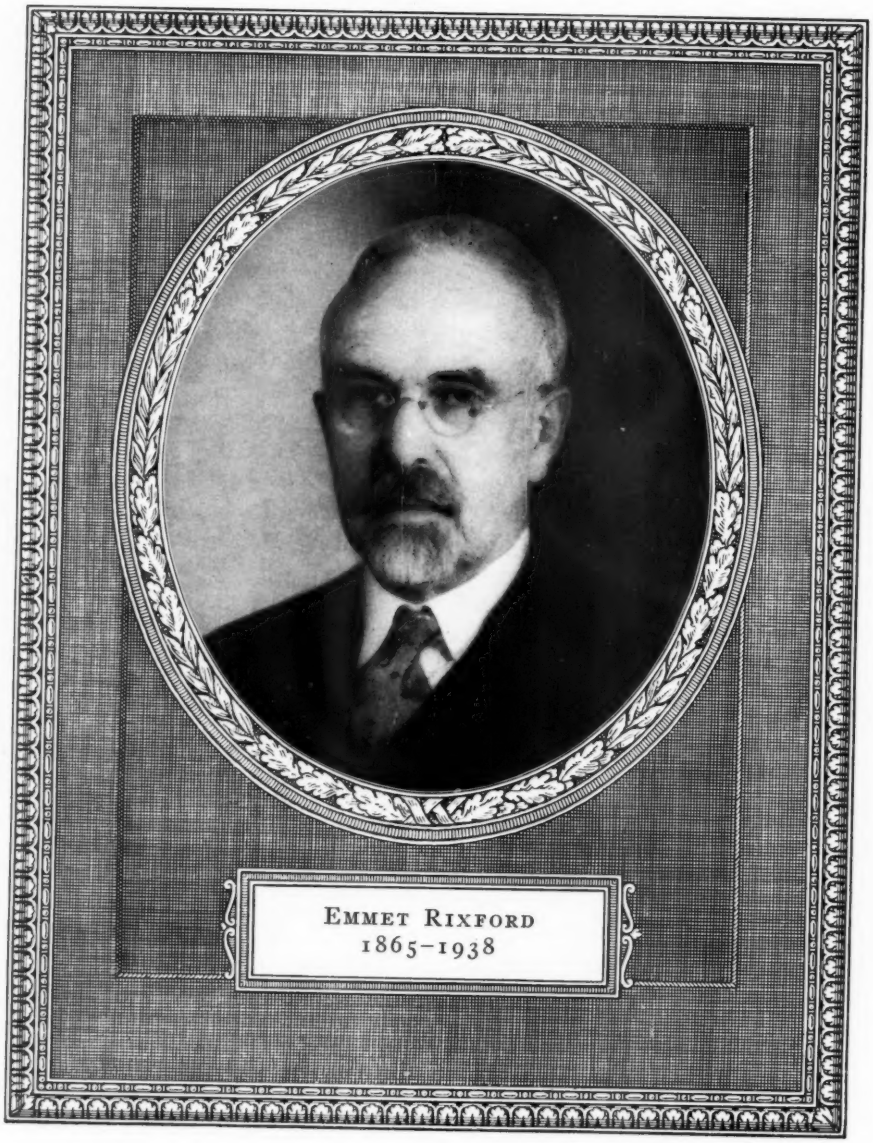
noted and with them symptoms of masculinity return. However, experience is accumulating which indicates that these tumors are usually of a low grade of malignancy. In most instances conservative surgery is justified especially when encapsulated arrhenoblastomas are encountered during the reproductive period.

Probably of much greater clinical importance is the granulosa-cell neoplasm which accounts for more than a tenth of all solid tumors of the ovary. It springs from a sexually differentiated cell, the granulosa cell, and, in contrast to the arrhenoblastoma, accentuates the state of feminity. This accentuation is best noticed among young individuals, for the tumor, through its hormone, estrogen, gives rise to precocious menstruation, hypertrophy of the breasts, growth of pubic and axillary hair and early union of the bony epiphyses. More than half of these tumors, however, are seen among women past the menopause. Here, recurrent periodic bleeding especially in the presence of an enlarged uterus should suggest to the keen clinician the possibility of a granulosa-cell tumor. Between the two extremes of life amenorrhea without masculinization, or amenorrhea followed by metrorrhagia are fairly constant symptoms. Both reflect a high fluctuating level of circulating estrogen, the product of the functioning tumor cells. These tumors have certain definite gross and microscopic features which may be recognized by the alert surgical pathologist in fresh frozen sections and in collaboration with the surgeon he can safely advise conservative management in certain cases. Prompt improvement of symptoms almost invariably follows operation. Young individuals have not infrequently become pregnant after local surgical removal of granulosa-cell tumors. Extreme radiosensitivity is also an important characteristic of these neoplasms.

Closely related to the granulosa-cell tumor on the one hand and the fibroma on the other are the theca-cell tumors of Loeffler and Priesel. Springing as they do from theca cells, it is not surprising that many of these tumors elaborate estrogen and produce a syndrome indistinguishable from that of granulosa-cell neoplasm. Theca-cell tumors usually manifest themselves following the menopause and are somewhat more malignant than the tumors described in the foregoing. Fortunately they may be easily recognized at operation by their dense consistency and yellow color. Conservatism in the treatment of this group is not so important because of the age of the patient and the possibility of recurrence of the neoplasm.

Functioning tumors of other endocrine organs have long been known to the surgical profession, and it is thus not surprising that functioning tumors of the ovary have been discovered at last. Such tumors of this organ are of importance to the embryologist in that they represent various phases of cellular differentiation and specialization. To the endocrinologist they furnish concrete evidence of hormonal production and its clinical effects. To the internist they present possibilities in the identification of tumors that formerly went unrecognized. Finally, to the surgeon and the pathologist there remains the interesting problem of confirming the clinical diagnosis and deciding on the proper line of treatment. The prognosis to the patient is far removed from that given in the days when these tumors were classed as atypical solid carcinomas and sarcomas of the ovary.

MALCOLM B. DOCKERTY.
VIRGIL S. COUNSELLER.



EMMET RIXFORD
1865–1938

UNIV. OF MICH.

MASTER SURGEONS OF AMERICA

EMMET RIXFORD

ON January 2, 1938, Emmet Rixford, professor of surgery, emeritus, at Stanford University Medical School, one time intimate associate of Dr. Levi Cooper Lane, died at the Peter Bent Brigham Hospital, Boston, of a coronary thrombosis, four days following an operation upon the bladder.

Dr. Rixford was born in Bedford, Quebec, of American parents, who journeyed to California in 1867, where the father became one of the state's distinguished pioneers. Accompanied by his wife and the two year old Emmet, he sailed from New York in a paddle steamer, crossed Nicaragua by canoe and donkey, and boarded a second paddle steamer for San Francisco. Though educated as an engineer, he became city editor of the *San Francisco Bulletin*, then partly owned by his uncle, Loring Pickering. Interested in horticulture, he was responsible for bringing into California a number of foreign trees, shrubs, and fruits, including the Smyrna fig, and several varieties of citrus fruits hardy enough to withstand the occasionally more rigorous climate of California. In the course of his duties as an active member of the State Horticultural Commission, he took his first ride in an aeroplane at 90. An advanced deafness caused his death by a train at 92.

The son, Emmet, graduated from the University of California in engineering in 1887, but was promptly diverted into medicine, taking his degree from Cooper Medical College in 1891. Together with Stanley Stillman, he became Dr. Levi Cooper Lane's assistant, later traveled as a graduate student in eastern and European clinics, was named adjunct professor of surgery at Cooper Medical College in 1893 and professor of surgery in 1898. When Cooper Medical College was taken over in 1909 by Stanford University as its medical department, he continued as professor of surgery and chief surgeon on the Stanford service at the San Francisco County Hospital, where he served continuously as visiting surgeon for 36 years. His Thursday morning "colloquia" were attended by numerous surgeons and many generations of students, who came to be instructed, as well as entertained, by this master of surgery. Resourceful and rapid in operating, quick and decisive in judgment, equipped with a mind abundantly laden with information at his immediate command, he made a brilliant teacher at the operating table.

His activity as an operator bridged the period between antiseptic and aseptic surgery, between drainage and non-drainage of wounds, but his facile mind quickly accepted and improved upon the rapidly advancing developments in surgery. His own words vividly describe this period:

"It is interesting to have lived through the period of the greatest and most rapid development in operative surgery the world has ever known, for it is not overstating the case when one claims that in the last fifteen years of the 19th century and the first fifteen of the 20th, greater progress was made in operative surgery than in all the centuries preceding, the direct result, of course, of the earlier discovery and promulgation of general, local, and regional anesthesia, and the gradual percolation and application of the principles of antisepsis of Lister and of asepsis of Macewen; I say gradual percolation of these principles, for it was difficult for the older generation to grasp the ideas and carry out the necessary practical details. For example, a very much up-to-date surgeon, enthusiastic about antisepsis, would conscientiously almost scrub the skin off his hands and soak them in bichloride and then, just before making his incision, would scratch his ear or blow his nose, adjust his spectacles or wipe his moustache and forget to sterilize his hands. I saw another surgeon bite off the end of a silk thread as would any seamstress to facilitate threading the needle, and one of our most noted local surgeons would hold his knife in his mouth when using other instruments in an operation. Practically speaking, then, the world had to wait for a new generation of surgeons to grow up before an aseptic technic could become automatic on a large scale."

Courageous in the face of technical difficulties that would defy the less experienced, he not infrequently scored a surgical triumph that astonished his associates. He early insisted upon a bacteriological and pathological study of his operative specimens, and was himself an excellent surgical pathologist. He was one of the first on this coast to employ the x-ray and with it to locate accurately, because of his engineering training, a foreign body in the brain, permitting its successful removal by his associate, Dr. Stanley Stillman.

His engineering training made him particularly adept also in the understanding of fractures and dislocations, and a number of his papers dealt in original manner with the mechanics of the production and treatment of the greenstick, buckling, torsion, and flexion fractures. His first paper in 1894 dealt with the symptoms and diagnosis of tuberculous disease of the joints. Subsequent papers covered the gamut of general surgery: the treatment of hernia, of goiter, of pancreatitis, of renal calculus, of gall stones, and of cancer in many sites; the rôle of industrial trauma in the development of cancer; the early history of the Pacific Coast medical schools and journals; the biographies of Cooper, Lane, and Huntington, pioneer master surgeons of California.

Quick to recognize in one of his early patients from the San Joaquin Valley that he was dealing with an unusual infection, he sent material to Professors Welch and Gilchrist of Johns Hopkins for further intensive study, which led subsequently to the recognition and description (by Rixford and Gilchrist in the first volume of the Johns Hopkins Hospital *Reports*, 1896) of a new disease, coccidioidal granuloma, also known as the San Joaquin Valley disease.

In recent years, the State Industrial Accident Commission relied greatly upon his judgment in the troublesome problems of industrial surgery, and he was often called as an expert witness. He rarely failed to impress the jury as to the correctness of his view.

National recognition of his ability came early: vice president of the American Surgical Association in 1905, and president in 1928; he was twice president of the San Francisco County Medical Society; he was a founder of the Pacific Coast Surgical Association, and became its president in 1932; he was long a member of the Society of Clinical Surgery and attended most of its meetings and accompanied its members on all but the last of its foreign tours. He was a fellow of the American College of Surgeons, a member of the Société Internationale de Chirurgie, the California Academy of Medicine, the California Academy of Science, and the California Horticultural Society. In 1928, at the request of Dr. Harvey Cushing, he served for three weeks as surgeon-in-chief *pro tem.*, of the Peter Bent Brigham Hospital in Boston, a significant honor shared on other occasions, among others, by such distinguished surgeons as Sir Charles Ballance, Professor Foerster of Breslau, Professor Gask of London, Professor Giertz of Stockholm, Professor Leriche of Strassburg, Sir D'Arcy Power of London, Professor Putti of Bologna, Sir Herbert Stiles and Sir David Wilkie of Edinburgh, Dean Lewis, Evarts Graham, Allen Whipple, and George Heuer of America.

A lifelong and paramount interest was the Lane Medical Library, the completeness and present position of which as one of the great medical libraries of the country are entirely due to his efforts. It was he who prevailed upon his classmates in 1891 to purchase a two-volume atlas of skin lesions, which really formed the nucleus for the later development of the present library. It was he who journeyed to the Surgeon General's Library on several occasions, found duplicates of important volumes, and was permitted to box and send them to San Francisco. It was through his perspicacity and friendship with Dr. Jacobi of New York, that he secured over 28,000 volumes of the early medical journals and greatly prized Paris theses which were found duplicated when the New York Academy and New York Hospital combined their libraries. The Lane Library, though named at his suggestion in honor of his chief, will be an enduring monument to his memory.

Although a distinguished scholar in his chosen field, Dr. Rixford's great charm lay in his extraordinary breadth of knowledge outside his professional calling. He was an authority on land snails and possessed one of the most complete collections in California. His achievements as an indefatigable mountain climber are forever commemorated by the designation of a 13,000-foot peak in the Kearsarge Range of the Southern Sierras as Mt. Rixford. His reputation as an authority on rose culture was nation-wide. More recently he had received from such distant places as Persia and Burma seeds of the "species" roses from

which all present stocks are descended, and was engaged in growing specimens for distribution to parks and horticultural societies. As skipper on the Sloop "Annie," brought around the Horn in the seventies, he won numerous races on San Francisco Bay, and was at one time designated Commodore of the Fleet. When "Annie's" day was finally done, she was reverently burnt at sea. As a young man he sang well and was a faithful member of St. Paul's choir. When the earthquake and fire of 1906 rendered many homeless, he was made chairman of a relief fund to help destitute physicians. Among the few things saved from his own burning home in that devastating fire were some armfuls of books which he buried in the yard. The Pacific Union, Bohemian, and Commonwealth Clubs of San Francisco claimed him as a member.

He is survived by his wife, Mrs. Louise Campbell Rixford; two sisters, Mrs. Geneve Rixford Sargeant, an artist, and Mrs. Caroline Byrd; a brother, Loring Pickering Rixford; a daughter, Mary Campbell; and three sons, Loring, Dr. Henry Covington Rixford, a surgeon of Stockton, California, and Dr. Emmet Lane Rixford, a surgeon in San Francisco.

His was an unusually active and useful life, full of zest for enjoyment, mingled with constant devoted service to his fellow men. No man, however poor, was ever denied the privilege of his skill. His service to the destitute sick of San Francisco is incalculable. When payment was possible, his requests were moderate. "No man whose life I have saved shall mortgage his remaining existence to me." He builded for himself an enviable monument of gratitude in the hearts of his fellow men. Many mourn his passing, few shall see his like again.

EMILE HOLMAN.

THE SURGEON'S LIBRARY

REVIEWS OF NEW BOOKS

IN the preface to the first edition of his book,[1] Magnuson states that it was written to meet the needs of the man who first sees the fracture. In the preface to the third edition, he reiterates this statement and emphasizes his purpose of calling attention to fundamental principles in diagnosis and treatment. Dr. Magnuson succeeds to a remarkable degree in accomplishing just what he intended to do.

The first 4 chapters discuss the fundamentals of diagnosis and treatment, the pathology and repair of fractures, the mechanism of reduction and maintenance of reduction, and fixation apparatus, both splints and plaster dressings. These preliminary chapters contain much helpful information and sound general principles of fundamental importance in fracture treatment.

The 21 following chapters discuss individual fractures in all regions of the body. As each region is taken up, the consideration of the individual fractures is preceded by brief but adequate remarks on the anatomy of the part and the manner in which muscle pull affects the displacement of the fragments. If joints are involved, joint movements are described and the effect which the various fractures have upon joint function is brought out. Each type of fracture is adequately discussed, usually in considerable detail. The subject matter throughout is sound, logical, and thoroughly conservative in viewpoint.

Complete as this book is, there are certain omissions which should be mentioned and some statements which will not find universal acceptance. In the description of plates for use in the internal fixation of fractures, no mention is made of vitallium, a metal which is being used very widely and with considerable satisfaction. In the description of fractures of the acetabulum, no mention is made of dislocation of the hip joint with fracture of the posterior superior rim of the acetabulum, a very common fracture today as a result of automobile accidents. In the description of treatment of central dislocation of the head of the femur, no mention is made of lateral traction by a Kirschner wire passed through the trochanter, combined with longitudinal traction; this is a very valuable form of treatment. In the description of the treatment of fractures of the shaft of the femur, no mention is made of the use of internal fixation; yet this is being very widely used today. Fractures of this lower articular surface of the tibia, sometimes called posterior marginal fracture, comprising about 19 per cent of all ankle fractures, are very inadequately discussed, in view of the fact that this is a very difficult fracture to reduce and maintain and results in marked disability if not adequately reduced. The statement that Volkmann's ischemic contracture is the result of tight splinting is today not generally accepted, as hemorrhage within the deep fascia is considered to be the most frequent cause of the condition.

The 2 final chapters deal with physical therapy and exercise in the treatment of fractures. This very much neglected part of fracture treatment is excellently and concisely covered and these chapters are full of helpful information and suggestions.

The general setup of the book is very pleasing. It reads easily, the type is large, and the illustrations are excellent and really explanatory. (It should be noted that Figure 217 is placed upside down.) The bibliography is very complete.

Dr. Magnuson, relying upon his broad experience and his extensive material, has succeeded in writing a book which attacks the problem of fractures and fracture treatment in a very direct and enlightening way. It is an excellent treatise which can be highly recommended not only to those who treat fractures occasionally but also to those who make fracture treatment an important part of their practice.

FRANK D. DICKSON.

IN its first edition *The Physiological Basis of Medical Practice* by Best and Taylor[2] rapidly became one of the foremost textbooks of physiology and has been widely used both by medical students and as a reference book. The second edition contains several revisions and the addition of a section on special sense physiology. In the preface the authors state that in the first edition they had not considered special sense physiology as being essential, but that they had been prevailed upon to include it in the second edition. It is certainly a worth while addition and makes the book complete. Like the first edition it is written in a style which is easy to read and understand, and each section is generously illustrated. With the recent additions it should continue to be one of the outstanding texts in the field.

J. ROSCOE MILLER.

THE text by Vinson[3] on diseases of the esophagus and their treatment is entirely new in its field. To the reviewer's knowledge it is the first attempt to present the subject in monographic style.

[1] FRACTURES. By Paul B. Magnuson, M.D., F.A.C.S. 3d rev. enl. ed. Philadelphia, Montreal, London: J. B. Lippincott Co., 1939.

[2] THE PHYSIOLOGICAL BASIS OF MEDICAL PRACTICE. By Charles Herbert Best, M.A., M.D., D.Sc., F.R.S., F.R.C.P., and Norman Burke Taylor, M.D., F.R.S., F.R.C.S., F.R.C.P., M.R.C.S., L.R.C.P. 2d ed. Baltimore: The Williams & Wilkins Co., 1939.

[3] THE DIAGNOSIS AND TREATMENT OF DISEASES OF THE ESOPHAGUS. By Porter P. Vinson, B.S., M.A., M.D., D.Sc., F.A.C.P. Springfield, Ill., and Baltimore, Md.: Charles C. Thomas, 1940.

The book is short, only 200 pages, but it is filled with worth while data and material collected from 20 years' experience and over 3,000 cases of abnormalities of the esophagus. One of the most interesting of the 16 chapters is given over to the general management of patients suffering from difficulty in swallowing—a subject of interest to the general practitioner as well as to the specialist in solving the many problems that arise during the management of these cases. Feeding is of paramount importance in patients with esophageal obstruction and Dr. Vinson has made many suggestions regarding this factor. Cardiospasm often presents difficulties, especially in the young, and one must know all the methods used in treatment. The relative merits and indications for the different methods are discussed. Chapters dealing with carcinoma of the esophagus, fungus infections, and foreign bodies as well as a chapter devoted to the use and possibilities of gastroscopy are included.

This book is easy to read, is presented in plain language, and very little space is devoted to detailed pathological description. The illustrations are practically all taken from photographs or x-ray films and serve as a ready guide to the descriptive text. The book is a welcome addition to the study of diseases of the esophagus, and is sure to be read with a great deal of interest by those specializing in diseases of the esophagus. JOHN F. DELPH.

THE book *Surgery of the Hand*[1] should be of great use to the practicing physician, for the author has clearly explained excellent methods for examination and care of injuries of the hands.

A complete chapter is devoted to nerve and tendon diagnosis and repair. The text has very pointedly brought out the economic loss resulting from poor management of injuries of the hands. The last part of the book concerns itself with the most common infections encountered and their management.

With both injuries and infections there are pertinent drawings to illustrate the important points. The final chapter on "Anesthetics" is excellent.

The author has used considerable space discussing amputation but has failed to outline the management of fascial space infections. The text is hardly detailed enough for student use but should be of great value to surgeons treating injuries and infections of the hands. HARVEY S. ALLEN.

THE original text of *Thomson and Miles' Manual of Surgery*,[2] now in its ninth edition, dates back to 1904. Twenty-eight members of the University of Edinburgh have collaborated with the two editors in producing the present edition. Volume 1 deals mainly with general surgical principles; Volume 2 is arranged on a regional basis with special emphasis upon diseases as they affect the various sections of the body.

The section on neurological surgery is especially noteworthy, as several chapters have been allotted to diseases of the central nervous system and have been handled in masterful style. The section on diseases of the thyroid gland is dealt with more efficiently than in most textbooks of surgery. It is interesting to note the definite Plummer influence regarding the so called "primary" and "secondary" hyperthyroidism. Diseases of the breast are investigated carefully, and the free use of pictures makes the section dealing with this subject more interesting. An excellent chapter on diseases of the peritoneum is presented, a subject which is treated more or less superficially in many textbooks of surgery.

While in general the chapter on appendicitis is satisfactory, yet the reviewer finds in it a fault that is so prevalent in other surgical volumes; namely, as a premise is quoted "The symptoms of appendicitis appear in a definite order, which is highly characteristic: (1) pain, (2) nausea, (3) vomiting, (4) tenderness and rigidity, (5) rise in pulse rate and temperature (Murphy)." Unfortunately, however, too many cases of appendicitis lack one or several of the so called cardinal symptoms, and too often medical students and men in the practice of medicine as well are led astray to the detriment of the patient because the categorical sequence of events is lacking. An excellent description of obstructive appendicitis is given which is too often lacking in surgical volumes. Likewise retrocecal and pelvic appendicitis, appendicitis in children and in patients past the fiftieth year are thoroughly examined. The subject of chronic appendicitis is given unusual prominence and is a worthy contribution.

While diseases of the stomach, duodenum, and intestines are rather sketchily covered, the subjects are handled fairly well. On the other hand, diseases of the gall bladder, common duct, and pancreas should receive more prominence.

Throughout the two volumes much emphasis is placed upon the pathological picture, and though treatment is given the signs and symptoms leading to the diagnosis of any given disease are placed uppermost. EARLE I. GREENE.

IN some 356 pages Dr. Riddell[3] has thoroughly covered the subject of blood transfusion as it is met in clinical use. He has omitted much recently accumulated data which are of interest only to those actively engaged in research. The sections on blood preservation and blood plasma are out of date, but this fact is undoubtedly due to the very active work going on in these fields.

Readers should be warned against adopting the policy of the voluntary donor agencies in England in which donors have Wassermann reactions done

[1] SURGERY OF THE HAND; SOME PRACTICAL ASPECTS. By John Harold Couch, M.A., M.B., F.R.C.S. (Edin.). Foreword by W. E. Gallie, M.D., F.R.C.S. (Eng.). Toronto: The University of Toronto Press, 1939.

[2] OXFORD MEDICAL PUBLICATIONS. THOMSON AND MILES' MANUAL OF SURGERY. By Alexander Miles, M.D., LL.D., F.R.C.S. (Ed.), and The Late Sir David Wilkie. Vols. 1 and 2. 9th ed. London: Oxford University Press, 1939.

[3] OXFORD MEDICAL PUBLICATIONS. BLOOD TRANSFUSION. By Victor Horsley Riddell, M.A., M.D. (Camb.), F.R.C.S. (Eng.). London: Oxford University Press, 1939.

after every tenth transfusion. Although possibly practical in a voluntary system, such methods are not acceptable in this country, especially since any medical student can be taught to perform flocculation tests easily and efficiently.

In general, the conclusions and recommendations of the author concerning problems not yet definitely settled are sound and logical.

THOMAS C. DOUGLASS.

IN epitome fashion *Industrial Hygiene*[1] covers the field of industrial medicine. Half of the content of this book of 661 pages devoted to clinical medicine, includes such subjects as physical examinations, tuberculosis, cardiac disorders, peripheral vascular diseases, dermatitis, eye injuries, traumatic surgery, neuropsychiatric problems, physical therapy, and rehabilitation. These chapters could well be incorporated in any general synopsis of medicine. Industrial hygiene, as commonly understood, is covered in chapters on silicosis, heavy metal intoxication, gases and fumes, lighting and atmosphere, while topics of general interest, such as scope of health service, the nurse in industry, railroad medical care, health education, compensation, statistical considerations of accidents and diseases, receive due attention.

Obviously such a replete volume must suffer because of brevity. Some compensation has resulted from a well chosen staff of authors. With many interrelated discussions there is some difference of opinion which is well tolerated.

This volume presents a review of the common medical problems met in industry. It is a good clinical review of medicine, presenting some of the aspects of the field of industrial hygiene. It may, with profit, be read by anyone interested in industrial practice.

EUGENE L. WALSH.

THE third edition of the *Mechanics of the Digestive Tract*,[2] which has been practically doubled in size and completely rewritten and extended in its scope of usefulness, is truly an introduction to gastroenterology. Dr. Alvarez's extensive background is physiological research and clinical medicine, combined with his genius in presenting his thoughts in a most readable style, is exemplified throughout the volume.

This book makes available for students, teachers, general practitioners, internists, and surgeons information about clinical physiology of the gastrointestinal tract which will be of great aid in sound diagnosis and treatment.

Today's conception of the control of the pylorus, innervation of the colon, and polarization of the bowel and gradients are presented in a crystallized manner. In addition, one finds the explanation of many of the practical problems of gastro-intestinal disease seen in daily practice such as hunger contractions, vomiting, ulcer pains, flatulence, reverse peristalsis and its symptoms, rate of progress of food residues, and movements of the diseased stomach.

To the tired and hurried practitioner, Alvarez has offered a summary at the end of each chapter where a brief answer to some question can be quickly obtained.

A chapter on technical methods and apparatus and visualized illustrations should be found very useful to laboratory workers.

The chapter on the source of books and articles of reading gives the student and young physician a quick entry into the several phases of gastroenterology and gastro-intestinal physiology. This chapter combined with an extensive bibliography will definitely aid in finding the most important papers, books, and review articles in the field.

I know of no other book that serves in such a unique manner as a real introduction to gastroenterology. I am sure after reading it that the application of its theories in the treatment of gastrointestinal disease in daily practice will be more scientific and less empirical.

CLIFFORD J. BARBORKA.

UNDER the title of *Cardiovascular-Renal Disease*[3] the Temple University collaborators discuss essential hypertension, arteriosclerosis, nephritis, and the other closely related conditions. Cardiovascular-renal disease as the chief cause of death in the individual over 45 years old deserves this concise, clear presentation, especially in view of recent drastic changes in our concept of this interrelationship. Goldblatt's discovery that ischemia of the kidney may be a large factor in the production of essential hypertension has led to a vast new literature on this entire subject. Evidence of the renal origin of hypertension is found in the preponderance of sclerosis of the kidney arterioles in cases of essential hypertension, and the occasional relief of hypertension by the removal of a unilateral pyelonephrosis.

The available material on glomerulonephritis, nephrosis, and toxemia of pregnancy has been digested and is presented to the student in a logical and easily assimilable form. As the authors state, "There is nothing in the entire presentation that can be termed original, except for the pooling of the medical, ophthalmological, and the pathological experience of the group." Chapters discussing the disease subgroups are followed by illustrative case studies with excellent photographs of the essential, gross, and microscopic pathology. Throughout, the importance of ophthalmoscopy is stressed, for "the ophthalmoscope is just as valuable an instrument in

[1] INDUSTRIAL HYGIENE. By various authors. Edited by A. J. Lanza, M.D., and J. A. Goldberg, M.A., Ph.D. New York, London, and Toronto: Oxford University Press, 1939.

[2] AN INTRODUCTION TO GASTRO-ENTEROLOGY. Being the third edition of the *Mechanics of the Digestive Tract*. By Walter C. Alvarez, M.D. New York and London: Paul B. Hoeber, Inc., 1940.

[3] CARDIOVASCULAR-RENAL DISEASE; A CLINICOPATHOLOGIC CORRELATION STUDY EMPHASIZING THE IMPORTANCE OF OPHTHALMOSCOPY. By Lawrence W. Smith, M.D., Edward Weiss, M.D., Walter I. Lillie, M.D., Frank W. Konzelmann, M.D., and Edwin S. Gault, M.D. New York and London: D. Appleton-Century Co., Inc., 1940.

the study of the patient with hypertension, including eclampsia, as renal functional tests are to the patient with nephritis." However, their classification of the retinal vascular changes is somewhat confusing and is less practicable than others in our experience.

One is impressed by the simplicity and clarity of the authors' presentation of the topic, cardiovascular-renal disease. This quality is no doubt partly due to the fact that the book is based on material from a scientific exhibit, an exhibit which was awarded the Frank Billings Gold Medal at the annual meeting of the American Medical Association in San Francisco in 1938.

All students of the vascular diseases probably will not find themselves in agreement with the views or interpretations which are held by this Philadelphia group, but the book may certainly be commended as being another attempt on the very live and difficult subject of cardiovascular disease.

M. HERBERT BARKER.

THE book, *Diverticula and Diverticulitis of the Intestine*,[1] is a compilation completely covering the subject of diverticula and diverticulitis of both small and large bowel. In four sections the author presents congenital diverticula, diverticula of the duodenum, diverticula of the jejunum, and diverticula of the large intestine. In each type of lesion he is able to present an abundance of material for illustration from both the anatomic and pathological viewpoint as well as to present x-ray films for diagnostic study.

Diverticula of the small bowel, including even Meckel's diverticula, are seldom encountered; serious surgical problems in connection with them are infrequent and for that reason one rarely finds a comprehensive presentation of these lesions such as is here given.

The section on diverticulosis and diverticulitis of the colon covers this subject very thoroughly, and because the disease is less frequent than malignancy, it is usually but incompletely presented in texts devoted to colon surgery. The author has written in detail the complications of diverticulitis, such as abscess, fistula, obstruction, etc., and has taken the pains to present the therapeutic problems involved in the treatment of these complications. To the surgeon not too experienced with these very serious lesions, this section of the book will prove very valuable.

The drawings and photographs, of which there are many, are excellent. Surgical technique is not illustrated. The subject matter is well written and clearly presented, and the reviewer regards this volume as a valuable reference work on a subject which causes many a surgical heartache.

J. R. BUCHBINDER.

[1] DIVERTICULA AND DIVERTICULITIS OF THE INTESTINE; THEIR PATHOLOGY, DIAGNOSIS, AND TREATMENT. By Harold B. Edwards, M.S. (Lond.), F.R.C.S. (Eng.). With foreword by Gordon Gordon-Taylor, O.B.E., M.S., F.R.C.S. Baltimore, Md.: The Williams & Wilkins Co., 1939.

IN response to a desire expressed by his students for an evaluation of the various methods for the surgical treatment of congenital cleft lip and palate, Dr. Vaughan[2] has succeeded, admirably, in compiling a book in which they will find "the subject concisely covered in one treatise."

In aiming to make the book "of practical value to the interested general surgeon, pediatric surgeon and the specialist in plastic and reconstructive surery," the author has done well to call attention to the unsuccessful operations and the difficulties which are to be overcome. This emphasis is important because operations to correct these deformities are judged, perhaps above all others, on the cosmetic and functional results.

The subject matter is set forth in good form, and the sections devoted to embryology, anatomy, and physiology are excellent.

In evaluating the various operations the author is most fair, and credit has been generously given. He, himself, has made worth while contributions to the plans for managing wide unilateral cleft palates and also the premaxilla in double cleft lip closure.

Prominence has been given to the matter of secondary operations and corrections, and the author is to be commended for the manner in which he has dealt with this subject.

Of especial interest is the chapter on palate lengthening and velopharyngeal closure, a development in cleft palate surgery tending toward greater functional perfection.

The importance of postoperative supervision of all repaired cleft palates is emphasized and attention is directed to speech training, orthodontic treatment to care for the developing alveolar arches and the teeth, and last, but not least, a desirable co-operation with the dentist who may be called upon to construct various appliances necessary to correction of deformities.

All in all this book is a splendid contribution, a *multum in parvo*, of use to all interested in cleft lip and palate correction. FREDERICK W. MERRIFIELD.

THE second edition of a most practical orthopedic handbook, *Handbook of Orthopædic Surgery* by Alfred Rives Shands,[3] differs from the first edition (1937) in several ways. It is a neater volume because of the improvement in the texture of paper. There are about 30 pages less in this edition and the volume is three-fourths as large. The text has been slightly altered to include new material and to omit irrelevant matter. The bibliography is excellent and has been brought up to date (July, 1939); it still ranks as one of the most modern orthopedic bibliographies available.

The illustrations, chiefly pen and ink drawings, are clear, descriptive, and to the point; many

[2] CONGENITAL CLEFT LIP, CLEFT PALATE AND ASSOCIATED NASAL DEFORMITIES. By Harold Stearns Vaughan, M.D., F.A.C.S., D.D.S. Philadelphia: Lea & Febiger, 1940.

[3] HANDBOOK OF ORTHOPÆDIC SURGERY. By Alfred Rives Shands, Jr., B.A., M.D. In collaboration with Richard Beverly Raney, B.A. M.D. St. Louis: The C. V. Mosby Co., 1940.

changes have been made in them from the first edition with additions, deletions, reductions in size, and new drawings. The instructive illustrations greatly enhance the value of the volume.

There are 24 chapters arranged in a manner ideal for teaching purposes. The authors express the views of contemporary orthopedic literature, textbooks, and teachers, in a concise factual manner.

The manuscript is well seasoned with theory and practical experience. There is no need to review the subject matter because it is pure fundamental orthopedic surgery in its complete scope.

Medical students, nurses, physical therapists, general practitioners, and orthopedic teachers will find this handbook the best available book on the subject for their requirements. SIDNEY SIDEMAN.

FOR many years the *New England Journal of Medicine* published reviews of recent contributions covering various branches of medicine. These presentations for the year 1939, compiled and edited by Robert N. Nye, are published as *Reports on Medical Progress*.[1]

The subject matter of these progress reports includes many of the commonly encountered problems of general medicine and surgery and the specialties. Fifty-two well chosen authors contribute to this work. In general, the reports are brief and accurate summaries of the more recent diagnostic and therapeutic aspects of the selected subjects. A limited number of references accompany each chapter. No attempt is made to include anything approaching a meticulous review of the literature.

The book is well bound and is printed in a type size that lends itself to easy reading. This type of year book will be of value not only to the general practitioner but also to the specialist who wishes to keep in contact with advances in fields of medicine other than his own. FRED FITZ.

FOR the most part *Shock, Blood Studies as a Guide to Therapy*[2] by John Scudder represents a study of one aspect of the complicated problem of shock, that of hydration and the rôle of potassium and the cortical hormone. The first part of the book deals with historical and experimental aspects and considers 4 theories of shock and 35 methods of treatment dating back to the days of John Hunter. A great deal of information is presented concerning the changes in the blood constituents with emphasis upon the potassium ion, its pharmacological action, and its increased concentration in the serum in certain types of shock. The importance of constant observation of the state of hydration of the patient and the aid given by cell volume, specific gravity of blood and plasma, and plasma protein determination is presented with a few illustrative cases. The importance of vascular dynamics of shock is less carefully considered. The author holds to the debatable view that vasoconstriction in shock is a harmful factor in promoting fluid loss and peripheral hemoconcentration. The important physiological rôle of vasoconstriction as one of the natural defense mechanisms of the body against fluid loss and shock is not mentioned.

The second part of the book consists chiefly of a case history presentation of 28 patients in various stages of circulatory collapse. They were treated with blood transfusions, salt solutions, and a proprietary cortical extract. The author believes that in shock with hyperpotassemia the use of sodium salts and cortical extract has been shown to be beneficial. He states that shock is not due to potassium poisoning alone but that alterations of potassium serve as a measure of profound cellular changes. He also suggests that the administration of large amounts of preserved whole blood high in potassium may be harmful in patients with hyperpotassemia.

The third part of the book deals with historical development and a bibliography. Brief abstracts on the conception and treatment of shock show the recent trend toward abandonment of the toxic theory, questioning of the nervous and corticoadrenal theory, and almost universal acceptance of the importance of circulating blood volume changes in the development of shock. Reports on the physiological and toxicological effects of potassium and on the function of the adrenal glands are also briefly abstracted.

This book has well emphasized the importance of a constant watch of the state of hydration of patients in vascular collapse. Although the presentation of the problem of shock is not entirely complete, information with regard to blood changes in shock and the suggestion of a therapeutic relationship between hyperpotassemia and cortical extract of the adrenal glands are presented. KEITH S. GRIMSON.

ALL too frequently books on the specialties, composed of chapters on special topics by various contributors, suffer the effects of redundance, repetition, overlapping of material, and even conflict of statements. From such faults *Injuries of the Skull, Brain and Spinal Cord*[3] is singularly free, which bespeaks a careful and competent editorship. The 23 contributors to this volume have co-ordinated successfully for the production of a well organized book which is certain to find widespread use and appeal, since there is a genuine need for such a reference source.

Trauma to the scalp, skull, meninges, brain, spine and cord is discussed in its surgical, neuro-psychiatric, and medico-legal aspects. The reviewer found the chapter on concussion and contusion of the brain, by C. P. Symonds, especially informative and useful in clarifying this elusive subject, most

[1] REPORTS ON MEDICAL PROGRESS, 1939; as published in the *New England Journal of Medicine*. Compiled and edited by Robert N. Nye, M.D. Boston: Little, Brown & Co., 1940.

[2] SHOCK; BLOOD STUDIES AS A GUIDE TO THERAPY. By John Scudder, M.D., Med.Sc.D., F.A.C.S. Philadelphia, Montreal, London: J. B. Lippincott Co., 1940.

[3] INJURIES OF THE SKULL, BRAIN AND SPINAL CORD; NEURO-PSYCHIATRIC, SURGICAL AND MEDICO-LEGAL ASPECTS. Edited by Samuel Brock. Baltimore: The Williams & Wilkins Co., 1940.

discussions of which are unsatisfactory. The etiology of post-traumatic neuroses is given a fresh and liberal treatment (p. 276), and though one need not especially adopt this particular theory of pathogenesis, sound as it may seem, any more than one need adopt the use of celluloid plates in the repair of cranial defects (p. 200) or other specific suggestions offered by the various contributors, yet each subject has been treated in a rational, modern manner according to the best experience of the individual. Fortunately, a minimum of case reports has been employed to illustrate the various topics of discussion. Elsberg's chapter on spinal cord injuries is an example of the outstanding accomplishment of this book, viz.: to be informative, to supply readily useful instruction, without being pedantic or arbitrary.

Each chapter is followed by a well selected bibliography. Most of these references are within the last decade, indicative of the recent interest in and importance of the subject of trauma to the central nervous system.

JOHN MARTIN.

A CAREFULLY prepared study of the problem of shock is presented in *Shock and Related Capillary Phenomena*[1] by Virgil H. Moon. The book is written primarily from a pathological point of view. The term "shock" is used in a broader sense than that usually considered in surgical literature and a relationship is brought out between the late or irreversible stages of surgical shock and death from other causes, such as infections and asphyxia. In this respect the detailed information relating to capillary atony and tissue anoxia is an important contribution to an understanding of shock.

[1]SHOCK AND RELATED CAPILLARY PHENOMENA. By Virgil H. Moon, A.B., M.Sc., M.D. London, New York, Toronto: Oxford University Press, 1938.

The contributory factors that lead to this later stage of tissue anoxia are considered. The author is well justified in his statement that these factors may be diverse. This is especially true in death in conditions other than surgical shock. In surgical and in traumatic shock the author defends the contention developed during and just after the World War that toxic agents absorbed from injured areas may be a major factor in the development of shock. The theory is offered that toxic injury to the capillaries may lead to capillary atony, reduced blood volume, reduced volume flow, reduced delivery of oxygen, and finally tissue anoxia which in turn directly or indirectly through toxic products further contribute to the original capillary atony. The experimental evidence for and against the theory of traumatic toxemia is presented, and the more generally accepted evidence against it and for blood or serum loss as a major factor is severely criticized. In this connection it should be stated that clinical experience is greatly reducing the incidence of surgical shock by adequate hemostasis, the employment of operation in bloodless fields under a tourniquet, early and adequate blood transfusions, and careful postoperative management of fluid balance is the best evidence that toxemia in these instances is not a major factor.

The factors of the late stage of shock are well considered in this carefully prepared and comprehensive book. The factors leading to this late stage remain complex and are probably multiple in many instances. The author, although probably overemphasizing the rôle of traumatic toxemia, has certainly produced a book on shock and its relation to capillary damage that is well worth reading.

KEITH GRIMSON.

BOOKS RECEIVED

Books received are acknowledged in this department, and such acknowledgment must be regarded as a sufficient return for the courtesy of the sender. Selections will be made for review in the interests of our readers and as space permits.

PRINCIPLES OF SURGICAL CARE; SHOCK AND OTHER PROBLEMS. By Alfred Blalock, M.D. St. Louis: The C. V. Mosby Co., 1940.

THE PRINCIPLES OF ANATOMY; AN INTRODUCTION TO HUMAN BIOLOGY. By A. A. Abbie, M.D., B.S., B.Sc., (Syd.), Ph.D. (Lond.). Sydney and London: Angus & Robertson Ltd., 1940.

FIVE YEAR STATISTICAL REPORT FROM THE CHRISTIE HOSPITAL AND HOLT RADIUM INSTITUTE, MANCHESTER, ON THE RESULTS OF RADIUM THERAPY FOR THE YEARS 1932 AND 1933. Stockport: Rowland Berry & Co. Ltd., 1939.

A TEXTBOOK OF HISTOLOGY. By Harvey Ernest Jordon, A.M., Ph.D. 8th ed. New York and London: D. Appleton-Century Co., Inc., 1940.

A HANDBOOK FOR DISSECTORS. By J. C. Boileau Grant and H. A. Cates. A Companion to *A Method of Anatomy*, by J. C. Boileau Grant. Baltimore: The Williams & Wilkins Co., 1940.

A METHOD OF ANATOMY, DESCRIPTIVE AND DEDUCTIVE. By J. C. Grant, M.C., M.B., Ch.B., F.R.C.S. (Edin.). 2d ed. Baltimore: The Williams and Wilkins Co., 1940.

THE SURGERY OF THE ALIMENTARY TRACT. By Sir Hugh Devine, M.S., F.R.A.C.S., F.A.C.S. Baltimore: The Williams & Wilkins Co., 1940.

THE ERA KEY TO THE USP XI & NF VI. Revised by Lyman D. Fonda. 5th ed. Newark, N. J.: The Haynes & George Co., Inc., 1939.

JAMES ANNESLEY (1780–1847). An Irishman, whose thirty-seven years as a military surgeon in India aided Britain to extend the Empire; a meticulous recorder of the symptoms of disease, remedies used and the results obtained; knighted by Queen Victoria.

James Annesley

1780-1847

UNIV. OF MICH.